

## ORIGINAL RESEARCH

# Comparison of RETREAT and CCFSS Scoring Systems for Risk Estimation of Hepatocellular Carcinoma Recurrence After Radical Resection

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### ABSTRACT

**Objective** • RETREAT and CCFSS are two scoring systems specifically designed to predict postoperative recurrence in hepatocellular carcinoma (HCC). RETREAT and CCFSS are scoring systems designed to predict postoperative recurrence in hepatocellular carcinoma (HCC). This study aims to evaluate and compare the prognostic performance of two scoring systems, RETREAT and CCFSS, for predicting tumor recurrence after radical resection in patients with hepatocellular carcinoma (HCC).

**Methods** • In this retrospective study, we analyzed the clinical data of 124 patients with HCC who underwent radical resection at our hospital between March 2017 and February 2020. The patients were categorized into a recurrence group ( $n = 41$ ) and a non-recurrence group ( $n = 83$ ) based on whether they experienced recurrence within 3 years of follow-up. Logistic regression analysis was conducted to compare the clinical characteristics between the two groups and identify factors associated with HCC recurrence. Additionally, we generated receiver operating characteristic (ROC) curves to evaluate the predictive value of the RETREAT and CCFSS scoring systems for predicting HCC recurrence after surgery.

**Results** • Significant differences ( $P < .05$ ) were found in the postoperative relapse-free survival time, HBsAg positivity, preoperative ALT  $\geq 40$  U/L, preoperative Alb  $< 40$  g/L, pericardial invasion, RETREAT score, and CCFSS score between the two groups. A multi-factor logistic regression analysis was performed between postoperative relapse in HCC patients and HBsAg positivity, preoperative ALT  $\geq 40$  U/L, preoperative Alb  $< 40$  g/L, pericardial invasion, RETREAT score, and CCFSS score grading as independent variables. The analysis revealed that HBsAg positivity ( $OR = 6.039$ , 95%CI: 2.994~12.182), preoperative ALT  $\geq 40$  U/L ( $OR = 3.738$ , 95%CI: 2.016-6.931), preoperative Alb  $< 40$  g/L

( $OR = 3.655$ , 95%CI: 2.083-6.415), envelope invasion ( $OR = 3.119$ , 95%CI: 1.922-5.061), RETREAT score ( $OR = 6.867$ , 95%CI: 3.204-14.719), and CCFSS score ( $OR = 3.228$ , 95%CI: 1.951-5.342) were significant factors influencing postoperative recurrence in HCC patients ( $P < .05$ ). The RETREAT score had an area under the curve (AUC) of 0.853, with a sensitivity of 89.23% and a specificity of 93.87% (95%CI: 0.7567-0.950), while the AUC of the CCFSS score for predicting postoperative recurrence in HCC patients was 0.741, with a sensitivity of 78.57% and a specificity of 60.71% (95%CI: 0.609-0.873). Among the factors analyzed, including postoperative relapse-free survival time, HBsAg positivity, preoperative ALT  $\geq 40$  U/L, preoperative Alb  $< 40$  g/L, pericardial invasion, RETREAT score, and CCFSS score, statistically significant differences were observed between the recurrence and non-recurrence groups ( $P < .05$ ).

**Conclusion** • The RETREAT score demonstrates higher efficacy compared to the CCFSS score in predicting postoperative recurrence in hepatocellular carcinoma (HCC) patients and can serve as a valuable tool for the prognostic evaluation of HCC patients who undergo radical resection. The RETREAT score's superiority can be attributed to its higher area under the curve (AUC) and improved sensitivity and specificity, which allow for better discrimination between positive and negative cases. This enhanced accuracy enables clinicians to make more informed decisions towards post-surgical management and treatment strategies, ultimately improving patient outcomes. Thus, the RETREAT score serves as a vital tool for personalized and targeted care towards HCC patients undergoing radical resection. (*Altern Ther Health Med.* 2023;29(8):694-698).

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### INTRODUCTION

Liver cancer is a globally prevalent malignant tumor, ranking sixth in incidence and third in malignancy-related

fatalities in China, with hepatocellular carcinoma (HCC) accounting for approximately 70%-90% of these deaths.<sup>1</sup> Surgery is the most effective clinical treatment for HCC; however, due to insidious symptoms in the early stage, most patients are diagnosed in the middle and late stages, with up to 70% of HCC patients undergoing radical resection relapsed, according to incomplete statistics.<sup>2</sup> However, due to the lack of early-stage symptoms, most patients are diagnosed during the advanced stages, thereby significantly affecting patients' survival and underscoring the importance of accurate postoperative recurrence prediction.<sup>3</sup> As such, many studies have focused on predicting recurrence in HCC

patients using scoring systems, such as the Cancer of the Liver Italian Program (CLIP) score,<sup>4</sup> the Risk Estimation of Tumor Recurrence After Transplantation (RET) score,<sup>5</sup> and the Cleveland Clinic Florida Scoring System (CCFSS).<sup>6</sup>

The RETREAT scoring system is designed to predict postoperative recurrence in hepatocellular carcinoma (HCC). This scoring system aims to assist physicians in predicting the risk of recurrence in HCC patients after curative resection. The RETREAT scoring system primarily relies on preoperative and postoperative clinical features, including positive hepatitis B surface antigen (HBsAg), preoperative serum alanine aminotransferase (ALT)  $\geq 40$  U/L, preoperative albumin (Alb)  $< 40$  g/L, and capsular invasion. These factors are considered to be associated with postoperative recurrence of HCC.<sup>7</sup> The CCFSS (Chinese Cancer and Fibrosis Staging System) scoring system is another scoring system used to evaluate postoperative recurrence in HCC patients. The RETREAT scoring system, emphasizing preoperative and postoperative clinical features, focuses on factors such as HBsAg positivity and capsular invasion, which are considered key predictors of HCC recurrence. In contrast, the CCFSS scoring system integrates liver fibrosis stage, microvascular invasion, and dyslipidemia, leveraging a comprehensive approach to assess recurrence risk. Compared to the RETREAT scoring system, the CCFSS scoring system primarily relies on factors such as liver fibrosis stage, microvascular invasion, and dyslipidemia to assess the risk of recurrence in HCC patients. This scoring system is based on extensive clinical research data, incorporating liver fibrosis stage and other relevant risk factors, and has undergone statistical analysis and validation.<sup>6</sup> However, few studies in China have utilized the RETREAT and CCFSS scores to predict HCC recurrence after radical resection. Hence, this study aimed to retrospectively evaluate and directly compare the predictive efficacy of the RETREAT and CCFSS scoring systems for postoperative recurrence in patients who underwent radical resection for HCC. To the best of our knowledge, there is a paucity of studies that have directly compared the RETREAT and CCFSS scoring systems for recurrence prediction in HCC following radical resection.

## PATIENTS AND METHODS

### Objects of study

The retrospective analysis involved clinical data from patients diagnosed with HCC and treated with radical resection at our hospital from March 2017 to February 2020. Inclusion criteria required that patients (i) have confirmed postoperative pathological findings of HCC, (ii) age above 18 years old, (iii) undergo radical resection, (iv) have no vascular invasion or preoperative extrahepatic metastases, (v) have Child-Pugh classification of grade A or B, and (vi) have complete clinical data with follow-up. Exclusion criteria were as follows: (i) recurrent HCC, (ii) postoperative pathologically confirmed mixed hepatocellular carcinoma or cholangiocarcinoma, (iii) combination with other malignant tumors, (iv) no preoperative radiotherapy or chemotherapy, (v) severe complications during

the perioperative period, and (vi) incomplete case or follow-up data. A total of 124 patients diagnosed with HCC were included in the study, comprising 110 males and 14 females aged 39-67 years, with a mean age of  $(49.56 \pm 6.87)$  years. The research adhered to the Declaration of Helsinki and was approved by the Hospital Ethics Committee.

### Observation indicators

The variables collected through the electronic medical record system included demographic data, laboratory findings, and clinicopathological data. (i) Demographic data: including age, gender, combined cirrhosis, recurrence-free survival time after surgery, hepatitis B surface antigen (HBsAg), body mass index (BMI), and Child-Pugh classification; (ii) laboratory findings: including preoperative serum alpha-fetoprotein (AFP) level, preoperative total bilirubin (TBil) level, preoperative albumin (Alb) level, preoperative white blood cell amount (WBC) and prothrombin time; The clinicopathological data included operation time, tumor number, maximum tumor diameter, envelope invasion, microvascular invasion, lymphovascular infiltration, tumor differentiation, tumor load (defined as the sum of maximum tumor diameter and number of live tumors), and the Barcelona Clinic Liver Cancer (BCLC) stage.

### Following-up

The study employed a combination of outpatient and telephone follow-up methods. After surgery, AFP levels were checked monthly for six months, while abdominal imaging was conducted every three months. MRI was employed if there was an expectation of tumor recurrence. Intra- and/or extrahepatic tumor recurrence after radical resection of hepatocellular carcinoma was confirmed using imaging techniques. Postoperative recurrence-free survival time was defined as the period from the surgery date to the time of postoperative tumor recurrence or the final follow-up appointment, including patients who died. The target date for the follow-up was February 28, 2023. Patients who did not experience recurrence during the 3-year retrospective clinical follow-up period were considered to have defaulted.

### Scoring Rules

**RETREAT score.**<sup>8</sup> (1) Preoperative AFP level (ng/ml): 0~20 is 0, 21~99 is 1, 100~999 is 2,  $\geq 1000$  is 3; (ii) Tumor load [sum of maximum surviving tumor diameter (cm) and number of surviving tumors]: 0 is 0, 1.1~4.9 is 1, 5.0~9.9 is 2,  $\geq 10$  is 3; (iii) Microvascular invasion: 2 points are available. The total RETREAT score was the sum of the scores of preoperative AFP level, tumor load and microvascular invasion, with 0~3 as a low risk of recurrence, 4 as a moderate risk of recurrence and 5 or more as a high risk of recurrence. The RETREAT score ranges from 0 to 3, indicating low, moderate, and high risks of recurrence, respectively.

**CCFSS score.**<sup>9</sup> (1) High risk of recurrence: one of the following three items was present, A. Maximum surviving tumor diameter  $\geq 5$  cm; B. Tumor differentiation was

hypofractionated; C. Lymphovascular infiltration was present; (2) Moderate risk of recurrence: one of the following two items was present, A. Maximum surviving tumor diameter < 5 cm; B. Tumor differentiation was moderate to high; (3) Low risk of recurrence: those who did not meet the criteria of high risk of recurrence and moderate risk of recurrence.

### Statistical analysis

Statistical Product and Service Solutions (SPSS) 25.0 (IBM, Armonk, NY, USA) was applied to analyze and process the obtained data. The measurement data were expressed and the comparison was done by *t* test; the count data were expressed as “n/%,” and the  $\chi^2$  test was used to compare the two groups. Factors that showed variability in comparison between groups but were not included in the RETREAT score and CCFSS score with the two sets of score points were used as independent variables, and postoperative recurrence of HCC was used as the dependent variable for binary as logistic regression analysis. Subject operating characteristic (ROC) curves were plotted to evaluate the predictive value of the RETREAT score and CCFSS score on recurrence after HCC surgery. The difference was considered statistically significant at  $P < .05$ .

## RESULTS

### Baseline characteristics and clinical features

In this study, 124 patients diagnosed with HCC were enrolled and divided into two groups: recurrence ( $n = 41$ ) and non-recurrence ( $n = 83$ ) based on their recurrence status three years following radical resection. Among the recurrence group, intrahepatic recurrence accounted for 87.80% (36/41) of cases, while the lung and abdomen accounted for 7.32% (3/41) and 4.88% (2/41), respectively. Statistical analysis revealed no significant differences ( $P > .05$ ) in age, gender, and combined cirrhosis between the two groups. Furthermore, no significant differences ( $P > .05$ ) were observed in postoperative relapse-free survival time, HBsAg-positive, preoperative alanine transaminase (ALT) 40 U/L, preoperative Alb 40g/L, envelope invasion, RETREAT score, and CCFSS score grading between patients in the relapse and non-relapse groups, shown as Table 1.

### Results of a multifactorial logistic regression analysis affecting postoperative recurrence in patients

In this study, postoperative recurrence in HCC patients was utilized as the dependent variable, while HBsAg positivity, preoperative ALT  $\geq 40$  U/L, preoperative Alb < 40 g/L, envelope invasion, RETREAT score, and CCFSS score grading were treated as independent factors. The results showed that HBsAg positivity ( $OR = 4.505$ , 95%  $CI$ : 2.215–9.162), preoperative ALT  $\geq 40$  U/L ( $OR = 3.738$ , 95%  $CI$ : 2.016–6.931), preoperative Alb < 40 g/L ( $OR = 3.655$ , 95%  $CI$ : 2.083–6.415), envelope invasion ( $OR = 3.119$ , 95%  $CI$ : 1.922–5.061), RETREAT score ( $OR = 6.867$ , 95%  $CI$ : 3.204–14.719), and CCFSS score ( $OR = 3.228$ , 95%  $CI$ : 1.951–5.342) were significant factors influencing postoperative recurrence in HCC patients ( $P < .05$ ). The results of the multifactorial

**Table 1.** Demographic characteristics and laboratory findings of patients

Characteristic	Recurrence (n = 41)	No Recurrence (n = 83)	$t/\chi^2$	P value
Age (years, $\bar{x} \pm s$ )	50.89 $\pm$ 6.45	49.23 $\pm$ 7.05	1.268	.207
Gender, male (n/%)	6/14.63	23/27.71	2.045	.153
Combined cirrhosis (n/%)	13/31.71	16/19.28	2.637	.124
Recurrence free survival time after surgery (month, $\bar{x} \pm s$ )	18.79 $\pm$ 1.85	32.32 $\pm$ 3.63	22.483	<.001
HBsAg positive (n/%)	34/82.93	37/44.58	16.491	<.001
BMI (kg/m <sup>2</sup> , $\bar{x} \pm s$ )	24.51 $\pm$ 0.86	24.28 $\pm$ 0.97	1.288	.200
Child-Pugh score (n/%)				
Class A	36/87.80	72/86.75	0.027	.869
Class B	5/12.20	11/13.25		
Preoperative ALT $\geq 40$ U/L	28/68.29	34/40.96	8.199	.004
Preoperative TBil (umol/L, $\bar{x} \pm s$ )	14.65 $\pm$ 2.33	13.97 $\pm$ 2.54	1.440	.152
Preoperative Alb < 40 g/L	33/80.49	26/63.41	26.591	<.001
Preoperative WBC (10 <sup>9</sup> /L, $\bar{x} \pm s$ )	5.54 $\pm$ 1.21	5.69 $\pm$ 1.25	0.635	.526
Prothrombin time (s, $\bar{x} \pm s$ )	12.65 $\pm$ 1.33	12.59 $\pm$ 1.48	0.219	.827
Surgery time (h, $\bar{x} \pm s$ )	3.89 $\pm$ 0.52	3.74 $\pm$ 0.38	1.823	.071
Number of tumors $\geq 2$ (n/%)	5/12.20	9/10.84	0.050	.823
Envelope invasion (n/%)	19/46.34	18/21.69	7.968	.005
R0 resection (n/%)	32/78.05	67/70.72	0.122	.727
BCLC classification (n/%)				
Stage 0	4/9.76	6/7.23	0.236	.627
Stage A	37/90.24	77/92.77		
RETREAT score (n/%)				
Low risk	2/4.88	74/89.16	10.520	<.001
Moderate risk	0/	8/9.64		
High risk	39/95.12	1/1.20		
CCFSS score (n/%)				
Low risk	13/31.71	63/75.90	6.769	<.001
Moderate risk	0/0.00	12/14.46		
High risk	28/68.29	8/9.64		

**Abbreviations:** HBsAg, Hepatitis B surface antigen; BMI, Body mass index; ALT, Alanine transaminase; TBil, Total bilirubin; Alb, Albumin; WBC, White blood cell.

**Table 2.** Assignment of a multifactorial analysis of postoperative recurrence in patients

Factor	Variables	Score standard
HBsAg	X1	Negative =0, positive =1
Preoperative ALT $\geq 40$ U/L	X2	Negative =0, positive =1
Preoperative Alb < 40 g/L	X3	Negative =0, positive =1
Envelope invasion	X4	Negative =0, positive =1
RETREAT score	X5	Low risk =1, moderate risk =2, high risk =3
CCFSS score	X6	Low risk =1, moderate risk =2, high risk =3

**Abbreviations:** HBsAg, Hepatitis B surface antigen; ALT, Alanine transaminase; Alb, Albumin.

**Table 3.** Results of a multifactorial logistic regression analysis affecting postoperative recurrence in patients

Factor	$\beta$ value	Wald $\chi^2$ value	P value	OR value	95% CI
HBsAg	1.798	25.231	<.001	6.039	2.994–12.182
Preoperative ALT $\geq 40$ U/L	1.319	17.522	<.001	3.738	2.016–6.931
Preoperative Alb < 40 g/L	1.296	20.394	<.001	3.655	2.083–6.415
Envelope invasion	1.138	21.209	<.001	3.119	1.922–5.061
RETREAT score	1.927	24.532	<.001	6.867	3.204–14.719
CCFSS score	1.172	20.792	<.001	3.228	1.951–5.342

**Abbreviations:** HBsAg, Hepatitis B surface antigen; ALT, Alanine transaminase; Alb, Albumin.

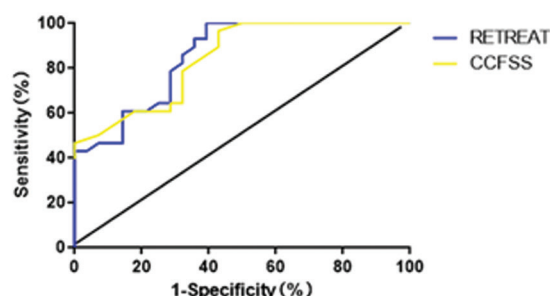
logistic regression analysis are presented in Table 2, while the ROC curve analysis results are shown in Figure 1.

### Results of ROC analysis of RETREAT score and CCFSS score for predicting postoperative recurrence

The results of ROC curve analysis showed that the area under the curve (AUC) of the RETREAT score for predicting postoperative recurrence in HCC patients was 0.853, with a sensitivity of 89.23% and specificity of 93.87% (95%  $CI$ : 0.7567–0.950); the AUC of the CCFSS score for predicting postoperative



**Figure 1.** ROC curves of RETREAT score, CCFSS score for predicting postoperative recurrence in HCC patients



recurrence in HCC patients was 0.741, with a sensitivity of 78.57% and specificity of 60.71% (95% CI: 0.609-0.873). See Figure 1. Higher AUC values indicate better predictive performance, and higher sensitivity and specificity values indicate better accuracy in identifying true positives and negatives

## DISCUSSION

Patients with hepatocellular carcinoma (HCC) typically do not present with clear symptom onset, and most cases are detected in the middle or advanced stages, with a high likelihood of recurrence following radical resection. Previous studies<sup>10,11</sup> have reported a 5-year recurrence rate of approximately 40%-70% following HCC surgery. In the current study, 41 cases of recurrence were observed at the 3-year follow-up point out of the 124 patients included, accounting for 33.06% of the cohort. Possible factors contributing to this relatively high recurrence rate include the relatively short follow-up time and potential geographical differences.

In this investigation, we conducted unilateral and multifactorial analyses to identify the factors contributing to postoperative recurrence in HCC patients. Our findings indicated that HBsAg positivity, preoperative alanine transaminase (ALT)  $\geq 40$  U/L, preoperative albumin (Alb)  $< 40$  g/L and envelope invasion were significant factors that affect postoperative recurrence in HCC patients. Hepatitis B surface antigen (HBsAg) positivity indicates an active or previous hepatitis B virus (HBV) infection. In patients with HCC, HBV infection is a significant risk factor for tumor development and recurrence. The presence of HBsAg suggests persistent viral replication, leading to chronic inflammation and liver damage. Chronic inflammation can promote the progression of liver cirrhosis and the development of HCC. Additionally, HBV DNA integration into the host genome can disrupt DNA repair mechanisms and contribute to genetic instability, increasing the likelihood of tumor recurrence after surgery. Alanine aminotransferase (ALT) is an enzyme primarily found in the liver. Elevated ALT levels suggest liver damage and inflammation. In patients with HCC, high ALT levels are associated with increased liver fibrosis and inflammation, which create a tumor-promoting microenvironment. Chronic inflammation can stimulate the proliferation of residual tumor cells, enhance angiogenesis, and impair immune surveillance, all of which contribute to postoperative recurrence. Albumin

(Alb) is a protein synthesized by the liver and plays a vital role in maintaining oncotic pressure and transporting various substances in the bloodstream. Low Alb levels, also known as hypoalbuminemia, indicate compromised liver function and poor nutritional status. Reduced Alb levels reflect the systemic response to liver dysfunction and chronic inflammation. Hypoalbuminemia is associated with an increased risk of postoperative complications, impaired wound healing, and reduced immune function, all of which can promote tumor recurrence. Envelope invasion refers to the infiltration of tumor cells into the surrounding vascular structures, such as blood vessels or lymphatic channels. This invasion signifies an aggressive tumor phenotype and an increased risk of tumor dissemination. When tumor cells invade the vascular system, they can disseminate to distant sites and form metastases. Envelope invasion is associated with a higher likelihood of residual tumor cells remaining after surgery, leading to an enhanced risk of postoperative recurrence. We propose that these outcomes could be attributed to the following factors: (i) Hepatitis B virus infection is a well-known risk factor for HCC, as it induces oxidative stress and increases DNA destruction by upregulating cytoplasmic cyclin A levels,<sup>12-13</sup> which in turn impairs liver function and heightens the risk of postoperative recurrence. (ii) ALT level is a crucial indicator of liver function. Impaired liver function affects metabolism and detoxification, leading to poor drug metabolism and exacerbating toxic side effects.<sup>14,15</sup> (iii) Alb is a vital protein component in the human body. Malnutrition can cause reduced synthesis of albumin, impairing immune function and reducing the number of immune cells that can clear hepatocellular carcinoma.<sup>16,17</sup> These factors, in turn, increase the risk of postoperative recurrence in HCC patients. The invasion of hepatocellular carcinoma tumor cells into the liver envelope is known to increase the risk of postoperative recurrence in HCC patients, as this process facilitates the invasion of tumor cells into surrounding liver tissues and blood vessels through the envelope factors.

The RETREAT score is a prognostic scoring system utilized to predict the recurrence of hepatocellular carcinoma (HCC) after surgery, incorporating tumor size, alpha-fetoprotein (AFP) level, and microvascular invasion. The preoperative AFP level is a crucial factor in assessing HCC prognosis.<sup>18</sup> Several studies have demonstrated that positive microvascular invasion is a significant factor contributing to postoperative recurrence and metastasis in HCC patients, leading to a considerably lower postoperative recurrence-free survival rate compared to patients with negative microvascular invasion.<sup>19-20</sup> On the other hand, the CCFSS score, which is based on pathological characteristics such as tumor diameter, differentiation degree, and lymphovascular infiltration, is infrequently employed in clinical practice. Both the RETREAT and CCFSS scoring systems take into account various clinical and pathological factors to predict postoperative recurrence in HCC patients. The inclusion of AFP levels in these scores enhances their predictive value by capturing the tumor's aggressiveness and potential for recurrence. However, it is crucial to interpret AFP levels alongside other

factors for a more comprehensive assessment of the risk of postoperative recurrence.

According to the results of our investigation, the RETREAT score demonstrated an AUC of 0.853, with an 89.23% sensitivity and a 93.87% specificity for postoperative recurrence in HCC patients. Conversely, the CCFSS score exhibited an AUC of 0.741, with a sensitivity of 78.57% and a specificity of 60.71%. Our findings suggest that the RETREAT score is more effective in predicting the postoperative recurrence of HCC when compared to the CCFSS score. This superiority may be attributed to excluding preoperative AFP levels from the CCFSS scoring system, despite numerous studies confirming that AFP levels are an independent risk factor for postoperative recurrence of HCC. The inclusion of this crucial indicator in the RETREAT score may be the reason for the higher sensitivity and specificity of the RETREAT score compared to the CCFSS score. The better sensitivity and specificity exhibited by the RETREAT score compared to the CCFSS score can be attributed to the inclusion of comprehensive factors such as tumor burden, microvascular invasion, histological grade, and AFP levels. The exclusion of certain factors, such as microvascular invasion and histological grade, from the CCFSS score may contribute to its slightly lower sensitivity, while the inclusion of liver cirrhosis may impact its specificity. However, further research and validation studies are necessary to establish the comparative performance of these scoring systems in diverse patient populations.

Consequently, the RETREAT score can be considered a valuable tool for predicting postoperative recurrence in HCC patients who have undergone radical resection and may assist in evaluating the prognosis of these patients. However, future research can improve the reliability and efficacy of statistical analysis by increasing the sample size. This can more accurately evaluate and compare the predictive effects of different scoring systems in different populations. The integration of the RETREAT score into clinical practice has the potential to improve treatment planning and patient outcomes in HCC patients undergoing radical resection. It allows for a more personalized approach to treatment, focusing on patients at higher risk who may benefit from additional interventions. By tailoring treatment plans based on individualized risk profiles, we can optimize therapeutic approaches and allocate healthcare resources more effectively, leading to improved long-term outcomes and quality of life for HCC patients. However, it is important to note that further research and validation studies are needed to establish the clinical utility and generalizability of the RETREAT score across different patient populations and healthcare settings.

In addition to the RETREAT scoring system and CCFSS system, other scoring systems' predictive abilities can also be studied for comparative analysis of their strengths, weaknesses, and scope of application. Based on existing research findings, we can further explore how to apply the RETREAT scoring system in clinical practice to improve the accuracy and effectiveness of decision support and treatment planning. This may involve developing new guidelines and procedures, training healthcare

professionals, and evaluating the long-term effects after implementation. Future research should focus on validating and external validating scoring systems, conducting comparative studies, evaluating long-term outcomes, incorporating genomic data, developing dynamic scoring systems, and performing cost-effectiveness analyses. By addressing these areas, we can further enhance the clinical utility and understanding of scoring systems for risk prediction in HCC patients undergoing radical resection, ultimately benefiting patient care and outcomes. To gain a more comprehensive understanding of scoring systems' predictive effects and clinical applications, long-term follow-up and retrospective studies can be conducted to assess their effectiveness in long-term treatment and prognosis.

## CONFLICT OF INTEREST

The authors have no potential conflicts of interest to report relevant to this article.

## AUTHOR CONTRIBUTIONS

SZ and YL designed the study and performed the experiments, XZ collected the data, CM analyzed the data, SZ and YL prepared the manuscript. All authors read and approved the final manuscript.

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## REFERENCES

- Zhang CH, Cheng Y, Zhang S, Fan J, Gao Q. Changing epidemiology of hepatocellular carcinoma in Asia. *Liver Int*. 2022;42(9):2029-2041. doi:10.1111/liv.15251
- Xiang YJ, Wang K, Yu HM, et al. Hazard rate for postoperative recurrence in patients with hepatocellular carcinoma at Barcelona Clinic Liver Cancer stage 0 or A1: A multicenter observational study. *Hepatol Res*. 2022;52(11):947-956. doi:10.1111/hepr.13811
- Zhang H, Liu F, Wen N, Li B, Wei Y. Patterns, timing, and predictors of recurrence after laparoscopic liver resection for hepatocellular carcinoma: results from a high-volume HPB center. *Surg Endosc*. 2022;36(2):1215-1223. doi:10.1007/s00464-021-08390-5
- Daniele B, Annunziata M, Barletta E, Tinessa V, Di Maio M; Cancer of the Liver Italian Program (CLIP) score for staging hepatocellular carcinoma. *Hepatol Res*. 2007;37 Suppl 2(S206-S209). doi:10.1111/j.1872-034X.2007.00186.x
- van Hooff MC, Sonneveld MJ, Ijzermans JN, et al. External Validation of the RETREAT Score for Prediction of Hepatocellular Carcinoma Recurrence after Liver Transplantation. *Cancers (Basel)*. 2022;14(3):630. doi:10.3390/cancers14030630
- Lai Q, Lesari S, Lerut JP. The impact of biological features for a better prediction of posttransplant hepatocellular cancer recurrence. *Curr Opin Organ Transplant*. 2022;27(4):305-311. doi:10.1097/MOT.0000000000000955
- Notaropolo A, Layese R, Magistri P, et al. Validation of the AFP model as a predictor of HCC recurrence in patients with viral hepatitis-related cirrhosis who had received a liver transplant for HCC. *J Hepatol*. 2017;66(3):552-559. doi:10.1016/j.jhep.2016.10.038
- Mehta N, Heimbach J, Harnois DM, et al. Validation of a Risk Estimation of Tumor Recurrence After Transplant (RETREAT) Score for Hepatocellular Carcinoma Recurrence After Liver Transplant. *JAMA Oncol*. 2017;3(4):493-500. doi:10.1001/jamaoncol.2016.5116
- Hasan B, Colak Y, Khalid RA, et al. Early Detection of Hepatocellular Carcinoma Recurrence in the Posttransplant Population: A Comparison of RETREAT and Cleveland Clinic Florida Scoring System. *Transplant Proc*. 2021;53(1):193-199. doi:10.1016/j.transproceed.2020.09.015
- Mehta N, Frenette C, Tabrizian P, et al. Downstaging Outcomes for Hepatocellular Carcinoma: Results From the Multicenter Evaluation of Reduction in Tumor Size before Liver Transplantation (MERITS-LT) Consortium. *Gastroenterology*. 2021;161(5):1502-1512. doi:10.1053/j.gastro.2021.07.033
- Zhu P, Liao W, Zhang WG, et al. A Prospective Study Using Propensity Score Matching to Compare Long-term Survival Outcomes After Robotic-assisted, Laparoscopic, or Open Liver Resection for Patients With BCLC Stage 0-A Hepatocellular Carcinoma. *Ann Surg*. 2023;277(1):e103-e111. doi:10.1097/SLA.0000000000005380
- Yun B, Ahn SH, Oh J, Yoon JH, Kim BK; Postoperative recurrence of liver cancer according to antiviral therapy for detectable hepatitis B viremia: A nationwide study. *Eur J Intern Med*. 2023;107(66-72). doi:10.1016/j.ejim.2022.10.026
- Li H. Hepatitis B virus PreS2 mutants in liver cancer patients. *Cell Mol Biol*. 2022;68(9):146-149. doi:10.14715/cmb/2022.68.9.23
- Zheng Y, Cai Q, Peng L, Sun S, Wang S, Zhou J. Related Factors of Hepatocellular Carcinoma Recurrence Associated With Hyperglycemia After Liver Transplantation. *Transplant Proc*. 2021;53(1):177-192. doi:10.1016/j.transproceed.2020.10.027
- Cao Q, Yang L, Zhou G, Hu Y; Clinical efficacy of laparoscopic radical hepatectomy and laparotomy for hepatocellular carcinoma and factors of postoperative recurrence. *Front Oncol*. 2022;13(116984). doi:10.3389/fonc.2023.1116984
- Liang Y, Zhang Z, Zhong D, et al; The prognostic significance of inflammation-immunity-nutrition score on postoperative survival and recurrence in hepatocellular carcinoma patients. *Front Oncol*. 2022;12(913731). doi:10.3389/fonc.2022.913731
- Zeng J, Zeng J, Lin K, et al. Development of a machine learning model to predict early recurrence for hepatocellular carcinoma after curative resection. *Hepatobiliary Surg Nutr*. 2022;11(2):176-187. doi:10.21037/hbsn-20-466
- Kim HI, An J, Kim JY, et al. Postresection Period-Specific Hazard of Recurrence as a Framework for Surveillance Strategy in Patients with Hepatocellular Carcinoma: A Multicenter Outcome Study. *Liver Cancer*. 2021;11(2):141-151. doi:10.1159/000518837
- Huang DS, Liu TT, Lu WT, et al. Comparison of portal and capsular microscopic vascular invasion in the outcomes of early HCC after curative resection. *Am J Cancer Res*. 2022;12(6):2659-2672. doi:10.14601/ajcr.220626
- Hu XS, Yang HY, Leng C, Zhang ZW. Postoperative outcomes and recurrence patterns of intermediate-stage hepatocellular carcinoma dictated by the sum of tumor size and number. *World J Gastroenterol*. 2022;28(44):6271-6281. doi:10.3748/wjg.v28.i44.6271