

# The Value of Preoperative Systemic Inflammatory Response index (SIRI) Combined with Albumin-Bilirubin Grading (ALBI) in Predicting Early Recurrence Following Curative Resection of Single Hepatocellular Carcinoma

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## Research Article

**Keywords:** systemic inflammatory response index, albumin-bilirubin grading, SIRI, ALBI, early recurrence, hepatocellular carcinoma, HCC, curative resection

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# Abstract

**Background:** This study was conducted to explore the risk factors for early recurrence of single hepatocellular carcinoma (HCC) following curative resection, and to evaluate the predictive value of systemic inflammatory response index (SIRI) combined with the albumin - bilirubin index (ALBI) for early recurrence of HCC following curative resection.

**Methods:** We retrospectively analyzed the clinical data of 233 patients with pathologically confirmed HCC who were admitted to the First Affiliated Hospital of Zhengzhou University from January 2015 to January 2018. The optimal cut-off values of alpha-fetoprotein, neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), SIRI, and ALBI were determined by receiver operating characteristic curve (ROC), and the predictive efficiency of each index was compared by area under curve (AUC). A Cox-proportional hazard regression model was used to analyze factors affecting early recurrence. Kaplan-Meier analysis was used to estimate the 2-year recurrence-free survival (RFS) rate of different factors.

**Results:** The AUC of SIRI for predicting early recurrence was 0.644, which was better than that of NLR, MLR, PLR, and SII. SIRI > 0.96, ALBI > -2.7, tumor diameter > 5 cm, and microvascular invasion (MVI) were risk factors for early recurrence after radical resection of HCC. The AUC of SIRI combined with ALBI was 0.759, which was better than that of single SIRI and ALBI. Combined with the above four risk factors, a new prognostic index was constructed, and the AUC for predicting early recurrence was 0.801.

**Conclusion:** SIRI, ALBI, MVI, and tumor diameter could be considered reliable predictors of early recurrence following curative resection of single HCC. Preoperative SIRI combined with ALBI possesses an important reference value in predicting early recurrence following radical resection of HCC. It is helpful for clinicians in identifying high-risk patients with early recurrence, actively carry out postoperative adjuvant treatment, and improving the prognosis of patients.

## Background

Primary liver cancer is the sixth most common malignant tumor and the fourth leading cause of tumor death worldwide [1]; it is the fourth most common malignant tumor and the second leading cause of tumor in China, of which hepatocellular carcinoma (HCC) accounts for 85–90% [2]. For patients with single HCC in Barcelona clinic liver cancer (BCLC) stage 0 or stage A, radical surgical resection is an important means of achieving long-term survival [3]. However, the recurrence and metastasis rate of patients with HCC is as high as 40–70% 5 years following radical resection, which is the leading cause of death [4–6]. Among them, early recurrence (recurrence within 2 years following surgery) accounts for more than 70% of recurrent tumors, and the prognosis is even worse [7]. Therefore, it is particularly important to evaluate the risks of early recurrence following radical resection of HCC, and to screen the population at high risk of early recurrence.

Tumor-related inflammation and immune responses are essential for the occurrence, development, angiogenesis, and metastasis of malignant tumors [8]. Several studies have shown that preoperative scores based on routine blood inflammatory indicators, such as neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), and platelet-to-lymphocyte ratio (PLR), affect the prognosis of HCC [5, 9, 10]. In 2016, Qi proposed a new inflammatory index based on peripheral blood lymphocytes, neutrophils, and monocytes, namely the systemic inflammatory response index (SIRI), which has been proven to predict the prognosis of many types of malignant tumors, such as pancreatic cancer, cervical cancer, esophageal gastric cancer, and breast cancer [11–14]. However, the value of SIRI in predicting early recurrence following radical resection of HCC has not been reported.

Liver function critically affects the treatment and prognosis of patients with HCC [15], it is particularly important to completely evaluate liver function. The Child-Pugh class has been widely applied in the evaluation of liver function and some tumor staging systems; however, the ability to evaluate liver function in patients with HCC with good liver reserve is limited, and is subjectively influenced by ascites and hepatic encephalopathy [16, 17]. Albumin - bilirubin index (ALBI) grade is a newly proposed alternative method for evaluating liver function based on albumin and bilirubin, which can avoid the influence of subjective factors and can further divide Child-Pugh A patients with HCC into two subgroups with different prognoses [18, 19]. Some studies have confirmed that the ALBI grade is better than the Child-Pugh grade in predicting the prognosis of patients with HCC [16, 17, 20] and proposed to combine it with conventional prognostic models [21, 22]. However, there are few studies on the value of ALBI in predicting early recurrence following radical resection of HCC.

This study aimed to explore the risk factors of early recurrence of HCC following radical resection, clarify the value of SIRI combined with ALBI in predicting early recurrence following radical resection of HCC, and construct a new prognostic index (PI) to predict early recurrence and evaluate its effect.

## Methods

### Inclusion and Exclusion Criteria

#### *Inclusion*

1. The ages of the patients were  $\geq 18$  years,
2. Child-Pugh grade A or B returned to grade A following hepatoprotective treatment before surgery,
3. HCC was diagnosed for the first time, and no antineoplastic therapy was administered before the operation,
4. Single tumors (BCLC stage 0 or stage A),
5. Radical resection of HCC,
6. No intervention, radiofrequency, radiotherapy, or systematic treatment was performed within 2 months following the operation.

## *Exclusion criteria*

1. Patients with incomplete clinical and pathological data,
2. Presence of hematological diseases or other malignant tumors,
3. Accompanied by acute or subacute infectious diseases,
4. Rupture of the liver cancer

## **General features**

This study retrospectively analyzed the data of 233 patients with HCC who underwent radical resection at the First Affiliated Hospital of Zhengzhou University from January 2015 to January 2018.

We collected the demographic data of the patients, including sex, age, and history of hypertension and diabetes. The laboratory data within one week before surgery, including hepatitis B surface antigen (HBsAg), alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin (Tbil), albumin (Alb), alpha-fetoprotein (AFP), peripheral blood leukocyte (WBC), neutrophils, monocytes, lymphocytes, and platelets, were obtained. In terms of tumor characteristics, tumor diameter, liver cirrhosis, microvascular invasion (MVI), and Edmondson-Steiner grade of HCC were considered as possible influencing factors following resection.

The calculation formula for each score was as follows: NLR= neutrophil count ( $\times 10^9$ ) / lymphocyte count ( $\times 10^9$ ), MLR= monocyte count ( $\times 10^9$ ) / lymphocyte count ( $\times 10^9$ ), PLR= platelet count ( $\times 10^9$ ) / lymphocyte count ( $\times 10^9$ ), SIRI= monocyte count ( $\times 10^9$ )  $\times$  neutrophil count ( $\times 10^9$  / L) / lymphocyte count ( $\times 10^9$  / L) / lymphocyte count ( $\times 10^9$  / L), ALBI=  $-0.085 \times \text{Alb} + 0.66 \times \text{Log}_{10} \text{Tbil}$  ( $\mu\text{mol/L}$ ).

## **Treatment and follow-up**

All 233 patients with HCC underwent curative resection. A total of 217 patients underwent laparotomy. Among them, 180 underwent non-anatomical resection and 37 underwent anatomical resection. The remaining 16 patients underwent laparoscopic hepatectomy.

## **Criteria for curative resection**

- (1) no macroscopic tumor thrombi were noted in the hepatic vein, portal vein, bile duct, and inferior vena cava
- (2) In the absence of adjacent organ involvement, portal lymph nodes, or distal metastases
- (3) The surgical margin and tumor boundary are  $> 1$  cm, or histologic examination of the cross section of the resected liver is free of residual tumor cells, which is a negative surgical margin [2]

## **Criteria of recurrence**

New intrahepatic or extrahepatic lesions were detected according to imaging examinations, including ultrasound, enhanced computed tomography (CT), magnetic resonance imaging (MRI), contrast-enhanced

ultrasound, and positron emission tomography-CT. Early recurrence was defined as recurrence within 2 years following radical resection of HCC.

## Follow-up

Postoperative follow-up was performed via telephone and outpatient review. The start time of follow-up was the start time of surgery, and the end point was the 2-year recurrence-free survival (RFS), which was defined as the date from the beginning of surgery to the date of tumor recurrence within 2 years. The last follow-up was performed on May 2021.

## Statistical analysis

All the analyses were performed using the IBM SPSS Statistics software (version 26). A receiver operating characteristic (ROC) curve was constructed to determine the optimal cut-off value. Continuous variables are presented as mean  $\pm$  standard deviation, and categorical variables as frequencies (%). A Cox-proportional hazard regression model was used to analyze the factors affecting the early recurrence of HCC. ROC curve analysis was used to evaluate the performance in predicting the early recurrence of HCC. Survival curves were plotted using the Kaplan–Meier method and compared using the log-rank test. Statistical significance was set at  $p < 0.05$ .

## Results

### *Clinical features*

A total of 233 patients were included in this study according to the inclusion and exclusion criteria. There were 184 men (79%) and 49 women (21%), with an average age of  $53.7 \pm 10.3$  y. Before the operation, 193 patients (82.8%) had complicated hepatitis B, and 202 patients (91.8%) had cirrhosis. All the patients had solitary tumors with an average diameter of  $5.0 \pm 3.0$  cm. All the patients had Child-Pugh grade A preoperatively. A total of 113 patients (48.5%) had early recurrence, 105 patients (92.9%) had intrahepatic recurrence, and 8 patients had extrahepatic recurrence, including 4 cases of lung metastasis, 2 cases of kidney metastasis, 1 case of omental metastasis, and 1 case of lymph node metastasis (Table 1).

Table 1  
General data of 233 patients with single  
hepatocellular carcinoma

	n (%)
Sex	

	n (%)
male	184(79%)
female	49(21%)
Age(years)	53.7±10.3
<60	162(69.5%)
≥60	71(30.5)
Hypertension	
no	187(80.3%)
yes	46(19.7%)
Diabetes	
no	214(91.8%)
yes	19(8.2%)
Liver cirrhosis	
yes	202(86.7%)
no	31(13.3%)
Surgical methods	
laparotomy	217(93.1%)
laparoscopic hepatectomy	16(6.9%)
Tumor diameter(cm)	5.0±3.0
≤5	136(58.4%)
>5	97(41.6%)
Edmondson-Steiner grade	180(77.3%)
I-II	53(22.7%)
III-IV	
Microvascular invasion	182(78.1%)
yes	51(21.9%)
no	

	n (%)
Non-early recurrence	120(51.5%)
Early recurrence	113(48.5%)
Intrahepatic recurrence	105(45.1%)
Lung metastasis	4(1.7%)
Kidney metastasis	2(0.9%)
Omental metastasis	1(0.4%)
Lymph node metastasis	1(0.4%)

*The optimal cut-off value and area under the curve (AUC) of AFP, ALBI and inflammatory indicators before surgery*

The ROC curve analysis demonstrated that AFP=35, ALBI=-2.7, SIRI=0.96, PLR=75.36, NLR=2.47 and MLR=0.3 were the optimal cut-off values. According to the threshold value of each indicator, patients with values less than or equal to the cut-off value were divided into the low-value group, while patients with values larger than the cut-off value were divided into the high-value group. The characteristics of the laboratory examination data after grouping are presented in Table 2. The prognostic value of these inflammatory indicators was further analyzed by comparing the AUC. The results demonstrated that the AUC of SIRI was larger than that of NLR, PLR, and MLR, indicating that the prognostic value of SIRI was better than that of NLR, PLR, and MLR (Table 3).

Table 2  
The characteristics of the laboratory examination data after grouping of 233 patients with HCC.

□□	frequencies (%) / mean ± standard deviation
<b>HBsAg</b>	193(82.8%)
+	40(17.2%)
-	
<b>ALT</b>	156(67%)
≤40	77(33%)
>40	
<b>AST</b>	161(69.1%)
≤40	72(30.9%)
>40	
<b>AFP</b>	121(51.9%)
<35	112(48.1%)
≥35	
<b>SIRI</b>	128(54.9%)
≤0.96	105(45.1%)
>0.96	
<b>ALBI</b>	113(48.5%)
≤-2.7	120(51.5%)
>-2.7	
<b>PLR</b>	97(41.6%)
≤75.36	136(58.4%)
>75.36	
<b>NLR</b>	168(72.1%)
≤2.47	65(27.9%)
>2.47	
<b>MLR</b>	127(54.5%)
≤0.3	106(45.5%)
>0.3	40.1±4.1

□□	frequencies (%) / mean ± standard deviation
Albumin (g/L)	12.9±6.6
Total bilirubin (μmol/L)	5.1±1.8
White blood cell count(×10 <sup>9</sup> )	134.4±62.5
Platelet count(×10 <sup>9</sup> )	3.1±1.3
Neutrophil count(×10 <sup>9</sup> )	1.5±0.6
Lymphocyte count(×10 <sup>9</sup> )	0.5±0.2
Monocyte count(×10 <sup>9</sup> )	

Table 3

The optimal cut-off value and area under the curve (AUC) of AFP, ALBI and inflammatory indicators before surgery.

variables	Cut-off value	sensitivity(%)	specificity(%)	Youden index	AUC (95% CI)
AFP	35	54.9	58.3	0.132	0.576 (0.502-0.649)
ALBI	-2.7	72.6	67.5	0.401	0.654 (0.582-0.726)
SIRI	0.96	63.7	72.5	0.362	0.644 (0.572-0.716)
PLR	75.36	63.7	46.7	0.104	0.528 (0.453-0.602)
NLR	2.47	40.7	84.2	0.249	0.637 (0.565-0.708)
MLR	0.3	53.1	63.3	0.164	0.587 (0.514-0.660)

*Univariate and multivariate analysis of early recurrence following radical resection of HCC.*

Cox univariate analysis showed that preoperative AFP, NLR, MLR, SIRI, ALBI, tumor diameter, Edmondson-Steiner grade, and microvascular invasion had significant effects on the early recurrence of HCC. The significant factors in the Cox univariate analysis were included in the Cox multivariate regression model. The results showed that SIRI, ALBI, tumor diameter, and microvascular invasion were independent influencing factors of early recurrence of HCC (Table 4).

Table 4

Univariate and multivariate analysis of early recurrence following radical resection of HCC.

Variables	Univariate analysis		Multivariate analysis	
	HR(95%CI)	P	HR (95%CI)	P
Gender	1.210(0.781-1.875)	0.394		
Age	1.278 (0.867-1.884)	0.215	2.167(1.293-3.633)	0.003
HBsAg	0.947(0.584-1.536)	0.827		0.001
ALT	1.082(0.734-1.596)	0.689	2.441(1.460-4.081)	0.038
AST	1.362(0.928-1.999)	0.114	1.497(1.023-2.190)	<0.001
AFP	1.509(1.042-2.186)	0.030		
SIRI	2.936(1.996-4.318)	<0.001	2.163(1.420-3.296)	
ALBI	3.161(2.095-4.768)	<0.001		
PLR	1.450(0.988-2.128)	0.058		
NLR	2.444(1.674-3.568)	<0.001		
MLR	1.494(1.033-2.163)	0.033		
Surgical method	0.812(0.378-1.746)	0.594		
Liver cirrhosis	0.925(0.537-1.593)	1.520	1.050-2.199	0.779
Tumor diameter	1.891(1.264-2.830)	0.026		
Edmondson-Steiner grading	3.104(2.102-4.585)	0.002		
Microvascular invasion		<0.001		

*Value of SIRIALBI combination in predicting early recurrence*

SIRI and ALBI were combined to divide patients into four groups: low SIRI+ low ALBI group, low SIRI+ high ALBI group, high SIRI+ low ALBI group, and high SIRI+ high ALBI group. ROC curves were constructed based on SIRI, ALBI, and SIRI-ALBI (Figure 1). By comparing their AUC, it was found that SIRI combined with ALBI was superior to SIRI and ALBI in predicting early recurrence of HCC (AUC=0.759,  $p < 0.001$ ) (Figure 1).

*Establishing a new PI for predicting early recurrence following curative resection of HCC*

The tumor diameter, SIRI, ALBI, and MVI were included in the Cox-proportional hazard regression model to fit the early recurrence risk function,  $h(t) = h_0 \exp (0.896 \times \text{SIRI} + 0.894 \times \text{ALBI} + 0.39 \times \text{tumor diameter} + 0.817 \times \text{MVI})$ . Constructing the (PI of early recurrence following curative resection of HCC,

$PI = 0.896 \times SIRI + 0.894 \times ALBI + 0.39 \times \text{tumor diameter} + 0.817 \times MVI$ ,  $SIRI > 0.96$ ,  $ALBI > -2.7$ , tumor diameter  $> 5$  cm, and MVI were all assigned 1; otherwise, 0 was assigned. The ROC curve was constructed to determine the optimal PI cut-off value of 1.25, and patients were divided into two groups: low-risk group ( $PI < 1.25$ ) and high-risk group ( $PI \geq 1.25$ ). ROC analysis was used to evaluate the predictive value of the prognostic index. The results showed that the AUC of PI was 0.801, indicating a high predictive value (Figure 1). Kaplan-Meier curve analysis showed that the 2-year RFS rate of the low-risk group was higher than that of the high-risk group ( $p < 0.001$ ) (Figure 2).

### *2-year RFS survival curve based on tumor diameter, SIRI, ALBI, and MVI*

The 2-year RFS survival curves of tumor diameter, MVI, SIRI, ALBI, and SIRI-ALBI were plotted using the Kaplan-Meier curves, and the differences in survival curves were tested using log-rank tests. The results demonstrated that patients with tumor diameter  $> 5$  cm,  $SIRI > 0.96$ ,  $ALBI > -2.7$ , and MVI had significantly lower recurrence-free survival at 2 years following surgery than those with tumor diameter  $\leq 5$  cm ( $p = 0.023$ ), no microvascular invasion ( $p < 0.001$ ),  $SIRI \leq 0.96$  ( $p < 0.001$ ), and  $ALBI \leq -2.7$  ( $p < 0.001$ ) (Figure 3). Patients with high SIRI-high ALBI had significantly lower relapse-free survival at 2 years following surgery than patients with low SIRI-low ALBI ( $p < 0.001$ ) (Figure 4).

## Discussion

At present, there is no consensus on the cut-off point for the time period for early recurrence following radical resection of HCC. Some clinical practice guidelines and most studies consider 2 years as the time cut-off point to distinguish early recurrence from late recurrence [3, 7, 23–29]. This study demonstrated that most patients (67.7%) showed recurrence within 2 years following surgery, and the risk of recurrence decreased and tended to level off after 2 years. Therefore, the time of early recurrence was set within 2 years following surgery in this study. Studies have confirmed that early recurrence and late recurrence are independent entities caused by different risk factors [6]. Early recurrence is considered to be intrahepatic or multicentric metastasis of the primary tumor, and is related to the invasiveness of the primary tumor, such as tumor number, tumor size, MVI, tumor differentiation, microsatellite nodules, and AFP [5, 6, 30], while late recurrence is mainly based on the etiology and background of liver cirrhosis [26, 28]. The results of multivariate analysis demonstrated that tumor diameter  $> 5$  cm and MVI were independent risk factors for early recurrence of HCC following radical resection; however, there was no significant difference in the degree of tumor differentiation.

As one of the most common indicators for the diagnosis and prognosis of HCC, AFP still has a controversial predictive value for early postoperative recurrence [26]. We found that AFP had a poor

predictive effect on early recurrence of HCC, with an AUC of only 0.576. Multivariate analysis also indicated that AFP could not be used as an independent factor influencing early recurrence of HCC following curative resection ( $p > 0.05$ ). This result is consistent with previous studies [5, 6, 30], whether AFP could be used as a predictor needs to be further verified.

In recent years, an increasing number of studies have demonstrated that inflammation plays an important role in the occurrence, development, and metastasis of malignant tumors [13, 25, 31]. The potential mechanisms could be that neutrophils are mainly concentrated in the peritumoral matrix of liver cancer tissues, [32] and can release angiogenic factors and inflammatory mediators, such as interleukin-1  $\beta$  (IL-1 $\beta$ ), interleukin-6 (IL-6), tumor necrosis factor- $\alpha$  (TNF- $\alpha$ ), and reactive oxygen species (ROS). In addition, neutrophils can inhibit the cytolytic activity of immune cells, which promotes the proliferation and metastasis of cancer cells [5, 9, 10, 31, 33]. Neutrophils and tumor-associated macrophages modulate the suppression of anti-tumor immunity by inhibiting the immune function of natural killer cells and T cells, leading to malignant progression [5]. Lymphocytes play an anticancer role in host immunity by inducing apoptosis and inhibiting the migration and invasion of cancer cells [10]. Platelets could protect tumor cells from natural killer cell-mediated lysis, and induce rapid activation of neutrophils, thereby promoting metastasis [28, 31].

The majority of HCC cases occur in the context of hepatitis and cirrhosis; therefore, inflammation is particularly significant in the process of its occurrence and development. Preoperative scoring systems based on peripheral inflammatory indicators, such as NLR, MLR, and PLR, have also been proven to be associated with the prognosis of HCC [5, 9, 10]. In 2016, Qi proposed a new inflammatory index based on peripheral blood lymphocytes, neutrophils, and monocytes, namely SIRI [11], and it has been proven to predict the prognosis of various malignant tumors, such as pancreatic cancer, cervical cancer, esophageal cancer of the stomach, and breast cancer [12–14]; however, its prognostic value in HCC has not been studied. In this study, patients with HCC complicated with hematological diseases and infectious diseases were excluded to prevent them from influencing routine blood indicators and interfere with the predictive value of early recurrence. The results showed that SIRI, NLR, and MLR could all be used to predict the early recurrence of single HCC following radical surgery, except for PLR. However, only SIRI was an independent risk factor for early postoperative recurrence. ROC curve analysis showed that among these indices, SIRI was of higher value in predicting early recurrence of single HCC following radical resection.

Child-Pugh grade was proposed by Child, Turcotte, and Paugh and used to evaluate the liver function of patients with liver cirrhosis and portal hypertension [34, 35]. Since then, it has been widely applied to evaluate the liver function reserve of patients with liver disease and has been applied in various tumor staging systems, including American Joint Committee on Cancer tumor/node/metastasis (AJCC TNM) staging, BCLC staging, and China liver cancer staging (CNLC) staging. The Child-Pugh score system is composed of five indicators: bilirubin, albumin, PT, ascites, and hepatic encephalopathy, in which ascites and hepatic encephalopathy are highly subjective, and the degree of ascites is correlated with albumin concentration, decreasing the ability to evaluate liver function reserve [16, 17]. In addition, with the

constant improvement of antiviral therapy and diagnosis of HCC, the number of patients with early HCC with good liver function has increased [15]. In this study, the preoperative Child-Pugh grades of 233 patients were all grade A; therefore, it cannot be applied to predict early recurrence of HCC.

ALBI, which was put forward in 2015, is a new index evaluating liver function in patients with HCC, especially those with good liver function reserve. [16, 18]. This index is only composed of bilirubin and albumin, which are both convenient and objective markers. Many studies have proved that its prediction effect is better than that of the Child-Pugh grade. In this study, 233 patients were divided into two groups by ALBI, and the ABLI > -2.7 group indicated that the prognosis was worse, which further confirmed the previous study.

We speculate that the combination of SIRI and ALBI can improve the prediction of early recurrence following curative resection, because the combination can simultaneously evaluate the inflammation, immune status, and liver function of patients with HCC. In this study, SIRI combined with ALBI was superior to SIRI or ALBI alone in predicting early recurrence in patients with single HCC. Patients in the low SIRI-low ALBI group had a lower 2-year recurrence-free survival rate. Therefore, preoperative SIRI combined with ALBI is an important reference value for predicting early recurrence of HCC following radical resection.

At present, there is no consensus on risk stratification tools for the early postoperative recurrence of HCC. Except for the AJCC-TNM tumor staging system in the United States, most tumor staging systems are not from surgically treated patients and do not consider MVI [26, 36]. This study showed that the area under the ROC curve for TNM staging was only 0.6, which could be due to the Child-Pugh scoring system used for liver function evaluation in the TNM system, while the Child-Pugh grading of 233 patients with HCC in this study was all grade A before surgery; thus, the difference in liver function between the two groups could not be effectively distinguished. In addition, the TNM-tumor staging system lacks evaluation of tumor-related inflammatory indicators. This study combined preoperative SIRI and ALBI to construct a new PI and confirmed that it is of higher value in predicting early postoperative recurrence.

There are certain limitations to this study. First, this study is a single-center retrospective study, which is prone to selection bias. Second, the cut-off value of each index was selected by the ROC curve. Different cut-off values could affect the final statistical results and warrants further verification. Therefore, further multicenter prospective studies should be conducted.

## Conclusions

Therefore, SIRI, ALBI, MVI, and tumor diameter could be considered reliable predictors of early recurrence following curative resection of single HCC. Preoperative SIRI combined with ALBI possesses an important reference value in predicting early recurrence following radical resection of HCC. It is helpful for clinicians in identifying high-risk patients with early recurrence, actively carry out postoperative adjuvant treatment, and improving the prognosis of patients.

# Abbreviations

HCC	hepatocellular carcinoma
BCLC	Barcelona clinic liver cancer
NLR	neutrophil-to-lymphocyte ratio
MLR	monocyte-to-lymphocyte ratio
PLR	platelet-to-lymphocyte ratio
SIRI	systemic inflammatory response index
ALBI	Albumin - bilirubin index
PI	prognostic index
HBsAg	hepatitis B surface antigen
ALT	alanine aminotransferase
AST	aspartate aminotransferase
Tbil	total bilirubin
Alb	albumin
AFP	alpha-fetoprotein
WBC	peripheral blood leukocyte
MVI	microvascular invasion
RFS	recurrence-free survival time
ROC	receiver-operating curve
AUC	area under the curve

# Declarations

## Ethics approval and consent to participate

This study was approved by the Ethics Committee of The First Affiliated Hospital of Zhengzhou University, No. 1 Jianshe East Road, Zhengzhou, Henan Province, China. All procedure performed in studies were in accordance with the Declaration of Helsinki.

## Consent for publication

This study was approved by the Ethics Committee of The First Affiliated Hospital of Zhengzhou University, No. 1 Jianshe East Road, Zhengzhou, Henan Province, China.

Since the study was conducted anonymously, no consent to publication by the patient was required.

## Availability of data and materials

The data that support the fundings of this study are available from the corresponding author (Yang Wu, MD, PhD) on request.

## Competing interests

All our authors have no conflicts of interest to disclose.

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## Authors' contributions

Yubin Fu and Penglei Ge put forward the idea of this study and collected, analyzed the data and wrote the article. Yubin Fu, Zhengkai Feng searched literatures. Penglei Ge, Lin Li and Yang Wu reviewed the manuscript and gave important professional advice. Yubin Fu, Zhengkai Feng, Jiahao Xue wrote the article. Yang Wu approved the final version of the article. Yubin Fu is the guarantor.

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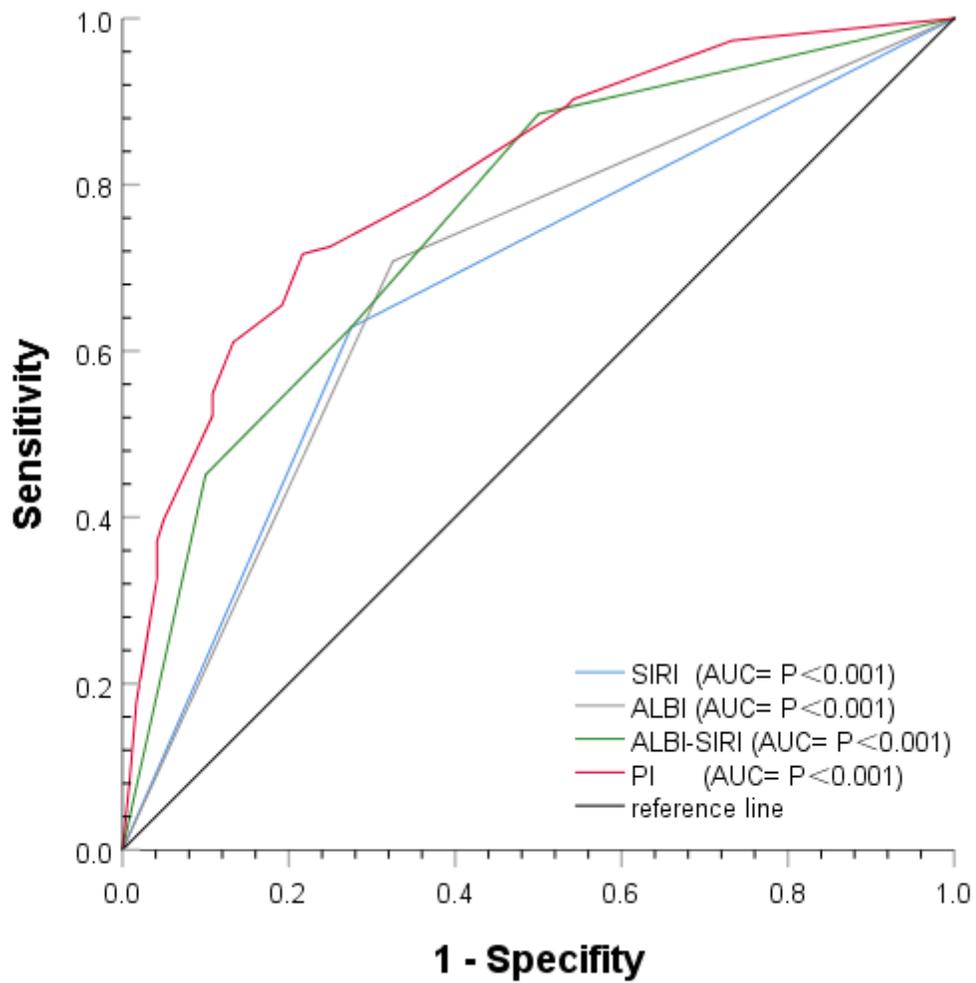
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## Figures



**Figure 1**

Comparison of systemic inflammatory response index (SIRS), albumin-bilirubin index (ALBI), ALBI-SIRS, and prognostic index (PI) in predicting early recurrence.

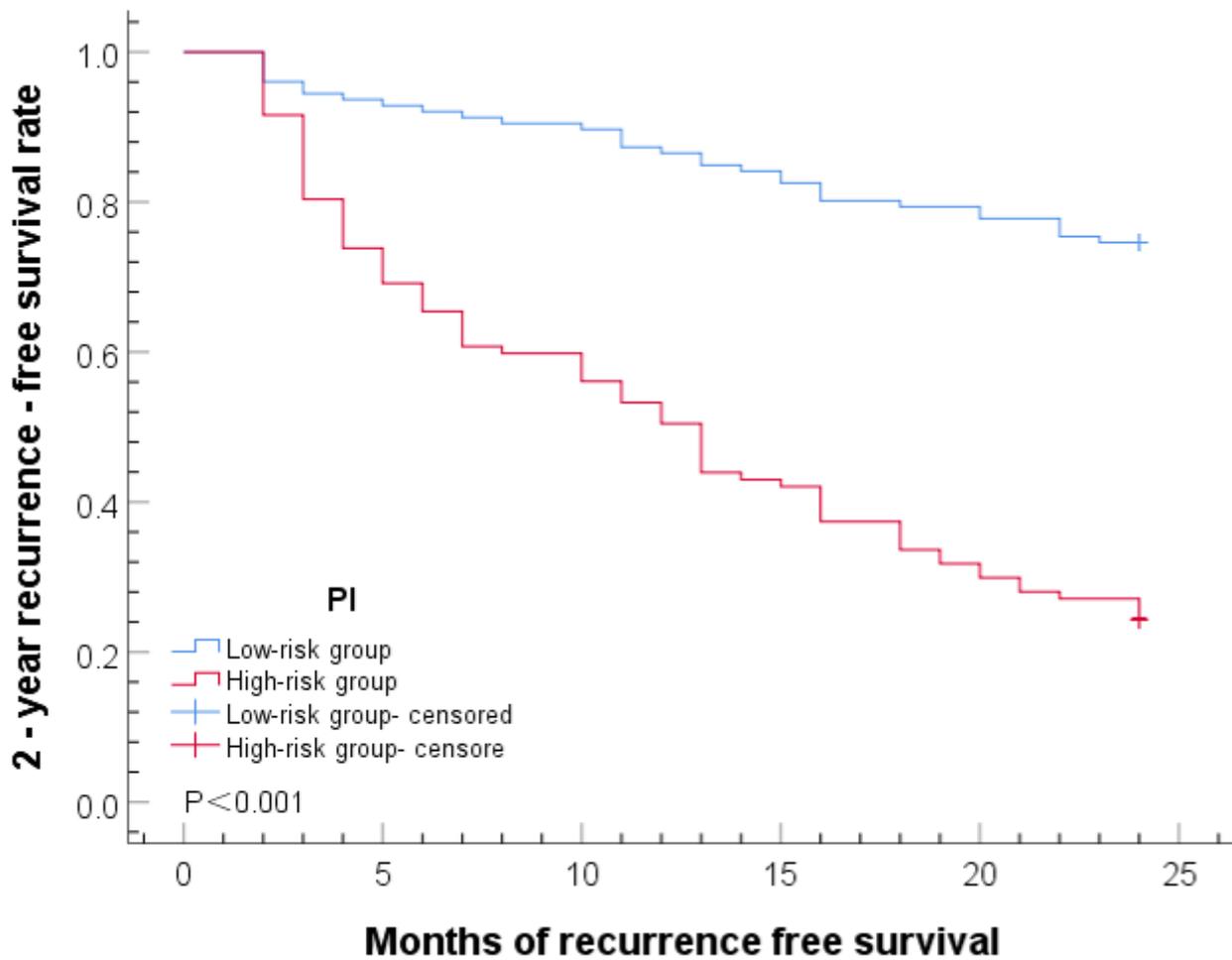
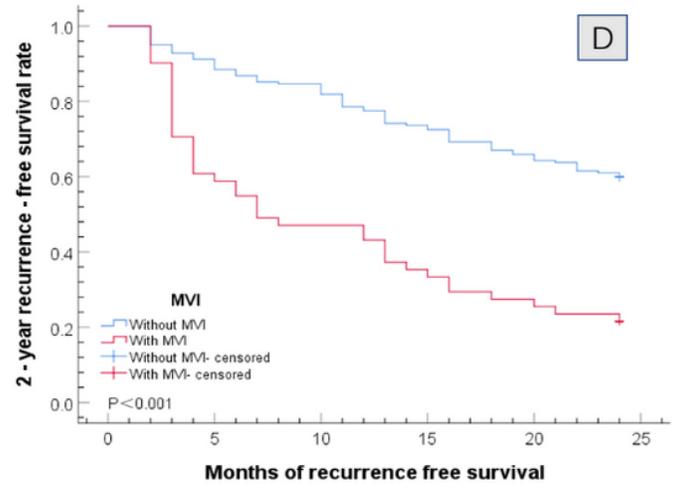
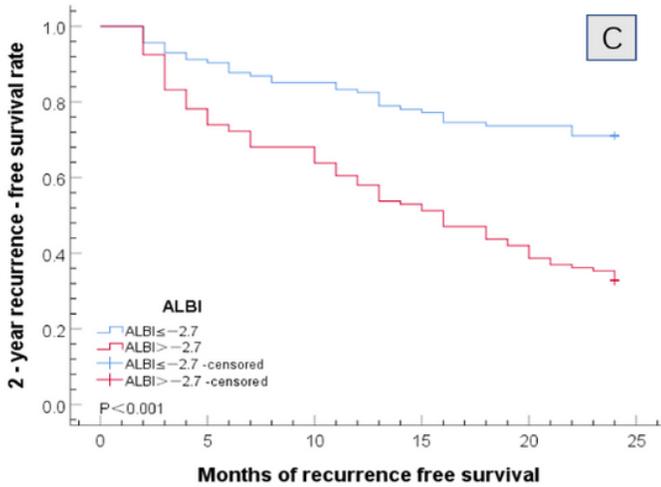
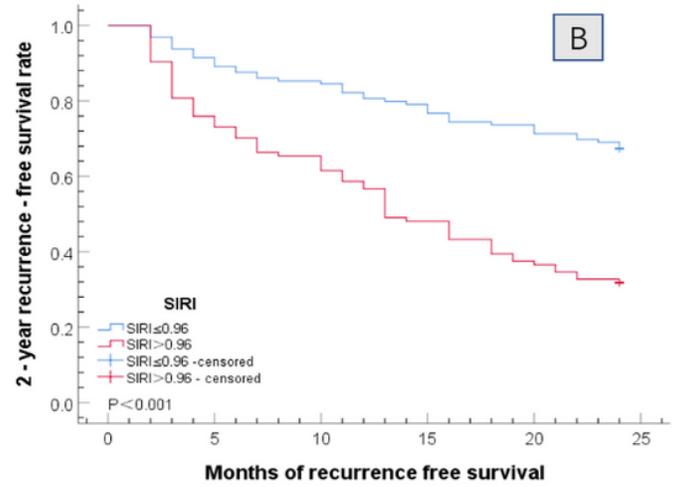
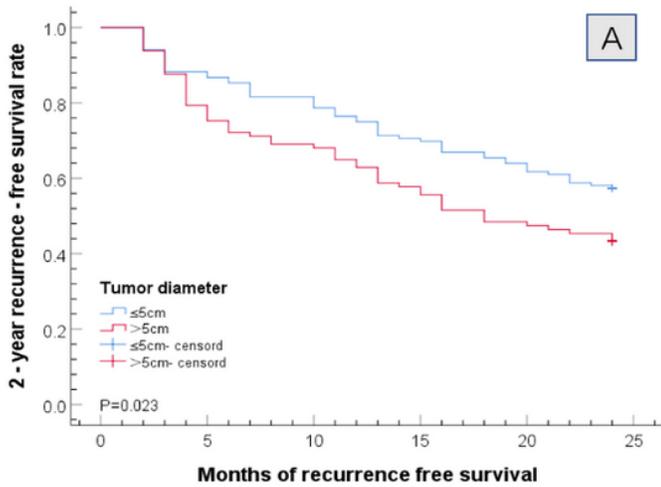


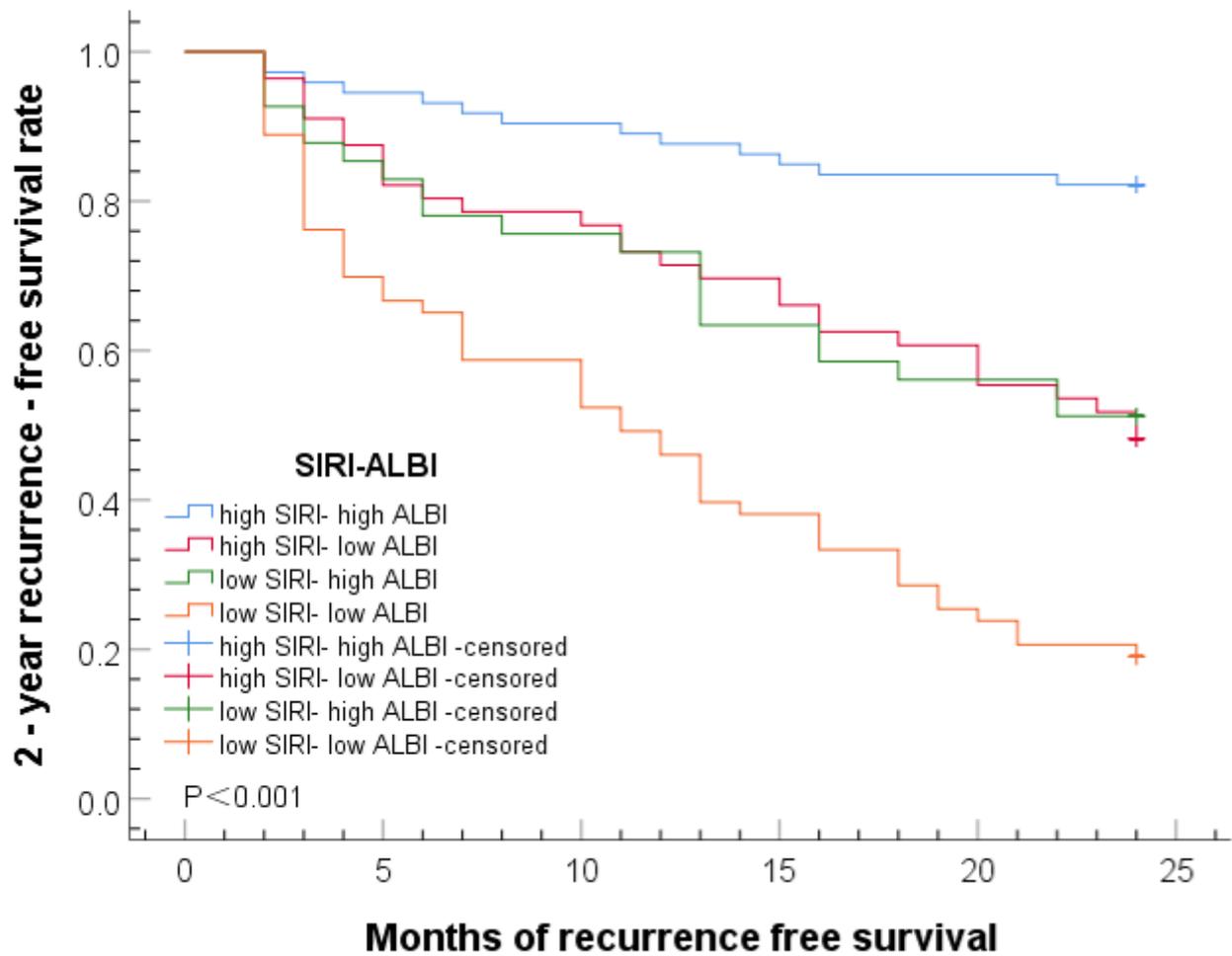
Figure 2

2-year recurrence-free survival curves of patients with low-risk group and high-risk group.



**Figure 3**

A) 2-year recurrence-free survival curves of patients with tumor diameter  $\leq 5$  cm and  $> 5$  cm. B) 2-year recurrence-free survival curves of patients with systemic inflammatory response index (SIRI)  $\leq 0.96$  and  $> 0.96$ . C) 2-year recurrence-free survival curves of patients with albumin-bilirubin index (ALBI)  $\leq -2.7$  and  $> -2.7$ . D) 2-year recurrence-free survival curves of patients with microvascular invasion (MVI).



**Figure 4**

2-year recurrence-free survival curves of patients with systemic inflammatory response index (SIRI) combined with albumin-bilirubin index (ALBI).