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ABOUT COVER

Peer Reviewer of *World Journal of Gastrointestinal Surgery*, Hideki Aoki, MD, PhD, Chief Doctor, Surgeon, Department of Surgery, Iwakuni Clinical Center, Iwakuni 740-8510, Japan. aoki.hideki.hy@mail.hosp.go.jp

AIMS AND SCOPE

The primary aim of *World Journal of Gastrointestinal Surgery* (*WJGS*, *World J Gastrointest Surg*) is to provide scholars and readers from various fields of gastrointestinal surgery with a platform to publish high-quality basic and clinical research articles and communicate their research findings online.

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ORIGINAL ARTICLE

Retrospective Study

Preoperative albumin-bilirubin score predicts short-term outcomes and long-term prognosis in colorectal cancer patients undergoing radical surgery

Yu-Hang Diao, Xin-Peng Shu, Can Tan, Li-Juan Wang, Yong Cheng

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Yu-Hang Diao, Xin-Peng Shu, Can Tan, Li-Juan Wang, Yong Cheng, Department of Gastrointestinal Surgery, The First Affiliated Hospital of Chongqing Medical University, Chongqing 400016, China

Co-first authors: Yu-Hang Diao and Xin-Peng Shu.

Corresponding author: Yong Cheng, PhD, Chief Doctor, Professor, Department of Gastrointestinal Surgery, The First Affiliated Hospital of Chongqing Medical University, No. 1 Youyi Road, Yuanjiagang, Yuzhong District, Chongqing 400016, China. chengyongcq@163.com

Abstract

BACKGROUND

The albumin-bilirubin (ALBI) score is a serum biochemical indicator of liver function and has been proven to have prognostic value in a variety of cancers. In colorectal cancer (CRC), a high ALBI score tends to be associated with poorer survival.

AIM

To investigate the correlation between the preoperative ALBI score and outcomes in CRC patients who underwent radical surgery.

METHODS

Patients who underwent radical CRC surgery between January 2011 and January 2020 at a single clinical center were included. The ALBI score was calculated by the formula (log10 bilirubin × 0.66) + (albumin × -0.085), and the cutoff value for grouping patients was -2.8. The short-term outcomes, overall survival (OS), and disease-free survival (DFS) were calculated.

RESULTS

A total of 4025 CRC patients who underwent radical surgery were enrolled in this study, and there were 1908 patients in the low ALBI group and 2117 patients in the high ALBI group. Cox regression analysis revealed that age, tumor size, tumor stage, ALBI score, and overall complications were independent risk factors for OS; age, tumor stage, ALBI score, and overall complications were identified as independent risk factors for DFS.

CONCLUSION
A high preoperative ALBI score is correlated with adverse short-term outcomes, and the ALBI score is an independent risk factor for OS and DFS in patients with CRC undergoing radical surgery.

Key Words: Colorectal cancer; Albumin-bilirubin score; Overall survival; Disease-free survival; Outcomes

Core Tip: The albumin-bilirubin (ALBI) scoring system is an objective and convenient method for evaluating liver function, and its prognostic value in a variety of cancers has been gradually recognized. In this study, patients who underwent radical surgery for colorectal cancer (CRC) were enrolled and divided into a high-ALBI score group (ALBI score > -2.8) and a low-ALBI score group (ALBI score ≤ -2.8) according to the cutoff calculated with X-tile software, and the results showed that the ALBI score is an independent risk factor for overall survival and disease-free survival in CRC patients undergoing radical resection.

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INTRODUCTION

Colorectal cancer (CRC) is the fourth most deadly cancer in the world, accounting for approximately 10% of total cancer-related deaths worldwide[1]. In the coming years, it is estimated that the incidence and mortality of CRC will continue to increase[2,3]. By 2040, the burden of CRC is expected to increase to 3.2 million new cases and 1.6 million related deaths [3]. Although there are different therapies available for CRC patients, including surgery, chemoradiotherapy, immunotherapy, and targeted therapy[4], the most important method for treating CRC is still radical surgery[5-7]. Nevertheless, even after undergoing radical surgery, the prognosis of CRC patients varies for many reasons, such as age[8], tumor stage [9,10], comorbidities[11-13], preoperative nutritional status[14], and postoperative complications[15,16]. Therefore, it is essential to comprehensively identify prognostic factors to improve the survival quality of these patients.

Albumin and bilirubin are serum biochemical indicators that reflect liver function to some extent[17,18]. The albumin-bilirubin (ALBI) scoring system, which is superior to the Child-Pugh grading system, was first described by Johnson *et al* [19] for assessing the liver function of patients with hepatocellular carcinoma (HCC). The prognostic utility of the system was gradually revealed in patients with HCC[20,21], gastric cancer[22,23], and pancreatic cancer[24,25]. Some studies have demonstrated that a higher ALBI score is also associated with a poor prognosis in CRC patients who underwent radical resection[26,27] and those who received chemotherapy[28] or targeted therapy[29].

Regarding the impact of the ALBI score on the short-term outcomes and long-term prognosis of CRC patients who underwent radical resection, Zhu *et al*[26] reported that the ALBI score is an independent risk factor for overall complications and overall survival (OS), and another study drew the same conclusion on OS[27]. However, limited by the sample size and retrospective nature of the study, the results above might not be accurate or reliable enough.

As a consequence, the purpose of this study was to investigate the correlation between the preoperative ALBI score and short-term outcomes as well as long-term prognosis in CRC patients who underwent radical surgery.

MATERIALS AND METHODS

Patient enrollment

Patients who underwent radical CRC surgery between January 2011 and January 2020 at a single clinical center were included. The study was approved by the ethics committee of our institution (The First Affiliated Hospital of Chongqing Medical University, 2024-011-01), and all patients signed an informed consent form. This study was conducted in accordance with the World Medical Association Declaration of Helsinki.

Inclusion and exclusion criteria

Patients who underwent primary CRC surgery were included in this study (n = 5473). The exclusion criteria were as follows: (1) Non-R0 CRC resection (n = 25); (2) incomplete clinical records (n = 323); (3) stage IV CRC (n = 875); and (4) incomplete total bilirubin/albumin examination (n = 225). Ultimately, a total of 4025 patients were included in this study (Figure 1).

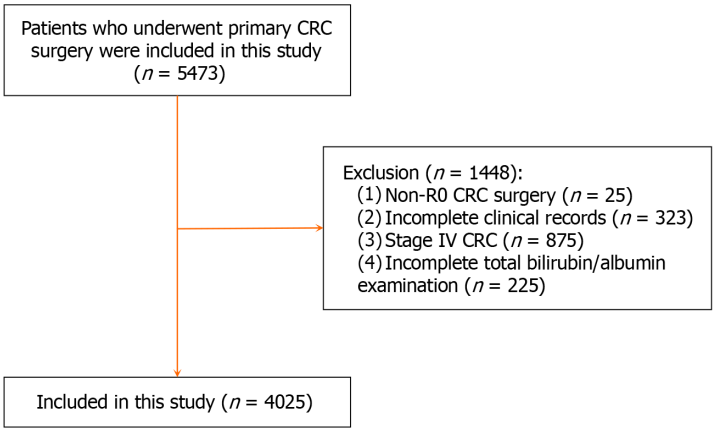

Figure 1 Flow chart of patient selection. CRC: Colorectal cancer.

Data collection

The baseline characteristics included the following: Age, sex, body mass index (BMI), smoking, drinking, hypertension, type 2 diabetes mellitus (T2DM), coronary heart disease (CHD), albumin level, total bilirubin level, ALBI, surgical history, tumor location, tumor-node-metastasis (TNM) stage, and tumor size. The short-term outcomes included operation time, intraoperative blood loss, blood transfusion, postoperative hospital stay, overall complications, and major complications. The long-term prognosis was predicted in terms of OS and disease-free survival (DFS). All the data were collected from the electronic medical records system or by outpatient visits and telephone interviews.

Definitions

TNM stage was determined according to the 8th edition of AJCC staging system[30]. Postoperative complications were classified on the basis of the Clavien–Dindo classification[31], and major complications were ≥ grade III. OS was defined as the time from surgery to death or loss to follow-up, and DFS was calculated from the date of surgery to the date of recurrence or death.

Treatment and follow-up

All patients underwent radical surgery according to standard principles. Patients were regularly followed up every 6 mo for the first three years and every year thereafter. An enhanced computed tomography scan was performed to determine whether the tumor had reoccurred.

ALBI score and groups

The ALBI score was calculated by the following formula: (log10 bilirubin × 0.66) + (albumin × -0.085), where bilirubin concentration is in μmol/L and albumin concentration is in g/L[19]. The cutoff that we adopted was -2.8 (according to the cutoff calculated with X-tile software)[32]. Then, the patients enrolled were divided into a high-ALBI score group (ALBI > -2.8) and a low-ALBI score group (ALBI ≤ -2.8).

Statistical analysis

Continuous variables are expressed as the mean ± SD, and an independent-sample *t*-test was used to compare the differences between the high-ALBI score group and the low-ALBI score group. Categorical variables are expressed as absolute values and percentages, and the chi-square test or Fisher's exact test was performed for comparisons. The Kaplan-Meier method was used to estimate OS and DFS, and the log-rank test was used to compare OS and DFS between the two groups at different tumor stages. Moreover, Cox regression analysis was performed to identify independent risk factors for OS and DFS. The data were analyzed using IBM SPSS Statistics for Windows, version 22.0 (IBM Corp., Armonk, NY, United States). A two-sided P value < 0.05 was considered to indicate statistical significance.

RESULTS

Characteristics of included patients

A total of 4025 CRC patients who underwent radical surgery were included in this study. According to the cutoff of the ALBI score, there were 1908 patients in the low ALBI group and 2117 in the high ALBI group. At baseline, the patients in the high ALBI group were older (P < 0.01) and had a lower BMI (P < 0.01), greater incidence of CHD (P < 0.01), greater total bilirubin concentration (P < 0.01), lower albumin concentration (P < 0.01), greater rate of open surgery (P < 0.01), and greater incidence of rectal cancer (P < 0.01) than those in the low ALBI group. In addition, fewer patients in the high ALBI group than in the low ALBI group had TNM stage I disease (P < 0.01) and tumors smaller than 5 cm (P < 0.01) (Table 1).

Table 1 Baseline information of high albumin-bilirubin group and low albumin-bilirubin group, *n* (%)

Characteristic	Low ALBI (1908)	High ALBI (2117)	*P* value
Age, years	60.0 ± 11.6	65.4 ± 12.1	< 0.01[a]
Sex			0.096
Male	1098 (57.5)	1273 (60.1)	
Female	801 (42.5)	844 (44.2)	
BMI, kg/m^2	23.1 ± 3.1	22.4 ± 3.3	< 0.01[a]
Smoking	707 (37.1)	813 (38.4)	0.378
Drinking	580 (30.4)	650 (30.7)	0.834
Hypertension	475 (24.9)	575 (27.2)	0.102
T2DM	225 (11.8)	273 (12.9)	0.289
CHD	55 (2.9)	117 (5.5)	< 0.01[a]
Albumin, g/L	44.3 ± 3.8	36.3 ± 4.1	< 0.01[a]
Total bilirubin, μmol/L	10.9 ± 5.4	12.0 ± 6.3	< 0.01[a]
ALBI	-3.1 ± 0.3	-2.4 ± 0.3	< 0.01[a]
Surgical history	446 (23.4)	500 (23.6)	0.856
Open surgery	163 (8.5)	365 (17.2)	< 0.01[a]
Tumor location			< 0.01[a]
Colon	1132 (59.3)	1005 (47.5)	
Rectum	776 (40.7)	1112 (52.5)	
TNM stage			< 0.01[a]
I	449 (23.5)	348 (16.4)	
II	770 (40.4)	956 (45.2)	
III	689 (36.1)	813 (38.4)	
Tumor size			< 0.01[a]
< 5 cm	1241 (65.0)	1106 (52.2)	
≥ 5 cm	667 (35.0)	1011 (47.8)	

[a]*P* < 0.05.

ALBI: Albumin-bilirubin; T2DM: Type 2 diabetes mellitus; BMI: Body mass index; CHD: Coronary heart disease.

Short-term outcomes

In the high ALBI group, patients had longer postoperative hospital stays ($P = 0.001$), greater intraoperative blood loss ($P = 0.001$), and more overall complications ($P < 0.01$) and more major complications ($P < 0.01$) than those in the low ALBI group, and the differences were all significant (Table 2).

Survival analysis

OS and DFS were observed by regular follow-up with a median follow-up period of 35 (1 to 114) mo. We compared DFS and OS between patients in the high ALBI group and the low ALBI group at different TNM stages. The high ALBI group had a worse OS for patients in all stages ($P < 0.01$), stage II ($P < 0.01$), and stage III ($P < 0.01$). Similarly, worse DFS was found in the high ALBI group for patients in all stages ($P < 0.01$), stage II ($P = 0.004$), and stage III ($P < 0.01$) (Figures 2 and 3).

Univariate and multivariate analysis for OS

For OS, in the univariate analysis, age (hazard ratio [HR]: 1.045, $P < 0.01$), BMI (HR: 0.952, $P < 0.01$), T2DM (HR: 1.280, $P = 0.048$), tumor size (HR: 1.464, $P < 0.01$), tumor stage (HR: 2.133, $P < 0.01$), ALBI score (HR: 1.900, $P < 0.01$), and overall complications (HR: 1.886, $P < 0.01$) were potential risk factors. Age (HR: 1.038, $P < 0.01$), tumor stage (HR: 2.099, $P < 0.01$), tumor size (HR: 1.231, $P = 0.017$), ALBI score (HR: 1.368, $P = 0.001$), and overall complications (HR: 1.619, $P < 0.01$) were found to be independent risk factors in the multivariate Cox analysis (Table 3).

Table 2 Short-term outcomes in high albumin-bilirubin group and low albumin-bilirubin group

Characteristic	Low ALBI (1908)	High ALBI (2117)	*P* value
Operation time (min)	223.6 ± 79.6	226.3 ± 81.7	0.295
Intraoperative blood loss (mL)	90.5 ± 122.5	104.4 ± 139.4	0.001[a]
Blood transfusion (%)	25 (1.3)	51 (2.4)	0.011
Postoperative hospital stay (d)	10.7 ± 9.4	11.6 ± 8.0	0.001[a]
Overall complications (%)	323 (16.9)	557 (26.3)	< 0.01[a]
Major complications (%)	32 (1.7)	61 (2.9)	< 0.01[a]

[a]$P < 0.05$.
ALBI: Albumin-bilirubin.

Table 3 Univariate and multivariate analysis of overall survival

Risk factor	Univariate analysis		Multivariate analysis	
	HR (95%CI)	*P* value	HR (95%CI)	*P* value
Age (years)	1.045 (1.037-1.053)	< 0.01[a]	1.038 (1.030-1.046)	< 0.01[a]
Sex (male/female)	0.873 (0.733-1.040)	0.128		
BMI (kg/m^2)	0.952 (0.926-0.978)	< 0.01[a]	0.984 (0.958-1.012)	0.263
T2DM (yes/no)	1.280 (1.002-1.633)	0.048[a]	0.981 (0.765-1.259)	0.883
Tumor site (colon/rectum)	1.173 (0.989-1.390)	0.066		
Tumor stage (III/II/I)	2.133 (1.864-2.440)	< 0.01[a]	2.099 (1.830-2.407)	< 0.01[a]
Smoking (yes/no)	1.055 (0.887-1.256)	0.543		
Drinking (yes/no)	1.025 (0.852-1.232)	0.796		
Hypertension (yes/no)	1.016 (0.836-1.234)	0.874		
Tumor size (≥ 5 cm/< 5 cm)	1.464 (1.235-1.736)	< 0.01[a]	1.231 (1.037-1.461)	0.017[a]
ALBI (high/low)	1.900 (1.587-2.274)	< 0.01[a]	1.368 (1.134-1.649)	0.001[a]
Overall complications (yes/no)	1.886 (1.580-2.252)	< 0.01[a]	1.619 (1.353-1.938)	< 0.01[a]

[a]$P < 0.05$.
BMI: Body mass index; T2DM: Type 2 diabetes mellitus, ALBI: Albumin-bilirubin.

Univariate and multivariate analysis for DFS

With regard to DFS, the univariate analysis demonstrated that age (HR: 1.033, $P < 0.01$), BMI (HR: 0.972, $P = 0.023$), tumor size (HR: 1.320, $P < 0.01$), tumor stage (HR: 2.046, $P < 0.01$), ALBI score (HR: 1.585, $P < 0.01$), and overall complications (HR: 1.686, $P < 0.01$) were significantly associated with worse DFS. Furthermore, age (HR: 1.027, $P < 0.01$), tumor stage (HR: 2.020, $P < 0.01$), ALBI score (HR: 1.504, $P < 0.01$), and overall complications (HR: 1.241, $P = 0.010$) were identified as independent risk factors in the multivariate Cox analysis (Table 4).

DISCUSSION

In this retrospective study, 4025 CRC patients who underwent radical surgery were enrolled. According to the cutoff of the ALBI score, there were 1908 patients in the low ALBI group and 2117 patients in the high ALBI group. In the high ALBI group, patients had longer postoperative hospital stays, more intraoperative blood loss, and more overall complications and major complications. Survival analysis revealed that patients in the high ALBI group had worse OS and DFS than patients in the low ALBI group with tumors of all TNM stages, stage II tumors, and stage III tumors. Furthermore, the preoperative ALBI score was identified as an independent risk factor for OS and DFS.

The prognostic value of the ALBI score for CRC patients has been reported in recent years. Abdel-Rahman[28] reported that a higher baseline ALBI score was an independent risk factor for OS ($P < 0.001$) and progression-free survival ($P < 0.001$) in CRC patients with liver metastasis after chemotherapy. Next, the association between the ALBI score and the

Table 4 Univariate and multivariate analysis of disease-free survival

Risk factor	Univariate analysis		Multivariate analysis	
	HR (95%CI)	*P* value	HR (95%CI)	*P* value
Age (years)	1.033 (1.026-1.040)	<0.01[a]	1.027 (1.020-1.035)	< 0.01[a]
Sex (male/female)	0.885 (0.757-1.035)	0.127		
BMI (kg/m^2)	0.972 (0.949-0.996)	0.023[a]	0.997 (0.973-1.021)	0.777
T2DM (yes/no)	1.129 (0.899-1.418)	0.297		
Tumor site (colon/ rectum)	1.095 (0.940-1.276)	0.245		
Tumor stage (III/II/I)	2.046 (1.816-2.305)	< 0.01[a]	2.020 (1.790-2.280)	< 0.01[a]
Smoking (yes/no)	1.037 (0.918-1.255)	0.374		
Drinking (yes/no)	1.029 (0.872-1.214)	0.736		
Hypertension (yes/no)	1.027 (0.863-1.223)	0.763		
Tumor size (≥ 5 cm/< 5 cm)	1.320 (1.133-1.538)	< 0.01[a]	1.134 (0.972-1.323)	0.110
ALBI (high/low)	1.585 (1.354-1.855)	< 0.01[a]	1.504 (1.276-1.774)	< 0.01[a]
Overall complications (yes/no)	1.686 (1.433-1.983)	< 0.01[a]	1.241 (1.053-1.463)	0.010[a]

[a]*P* < 0.05.

BMI: Body mass index; T2DM: Type 2 diabetes mellitus, ALBI: Albumin-bilirubin.

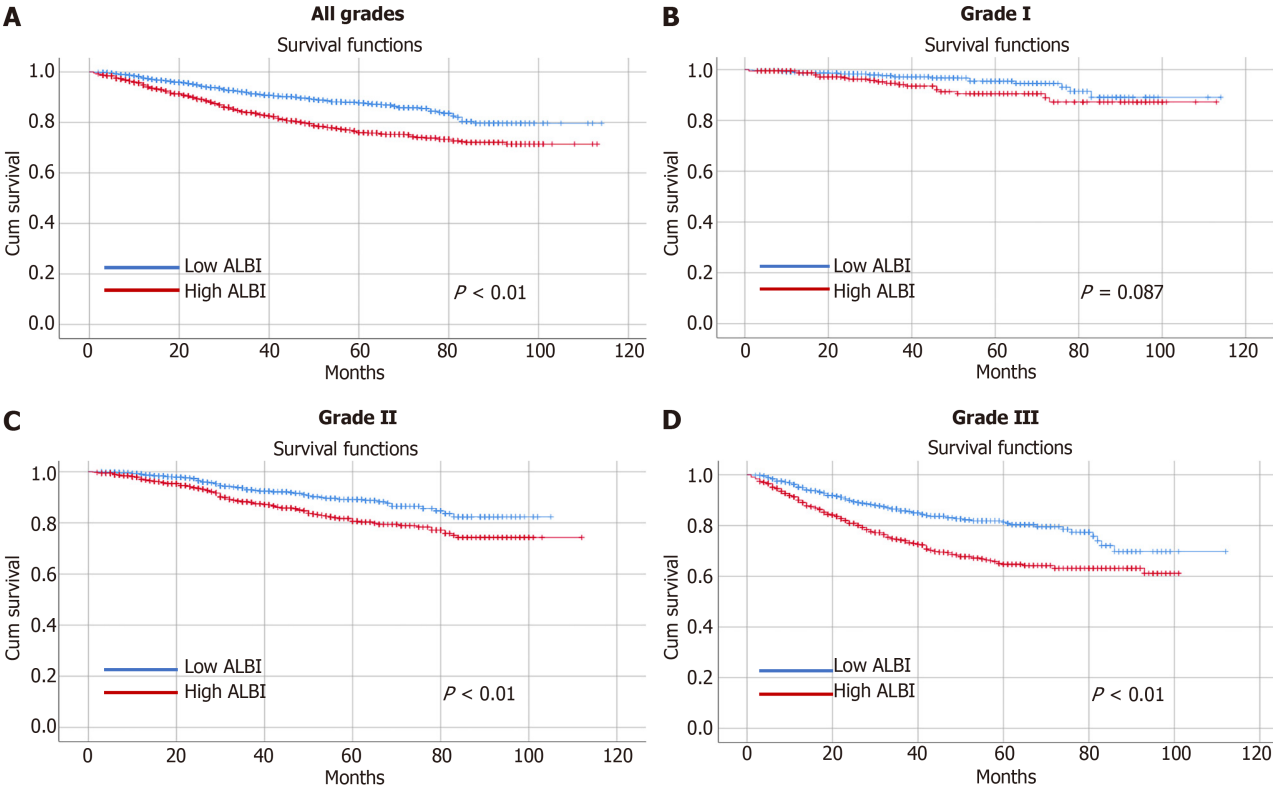

Figure 2 Kaplan-Meier survival curve analysis for impact of preoperative albumin-bilirubin score on overall survival of patients in all tumor-node-metastasis stages, stage I, stage II, and stage III. A: All tumor-node-metastasis stages; B: Stage I; C: Stage II; D: Stage III. ALBI: Albumin-bilirubin.

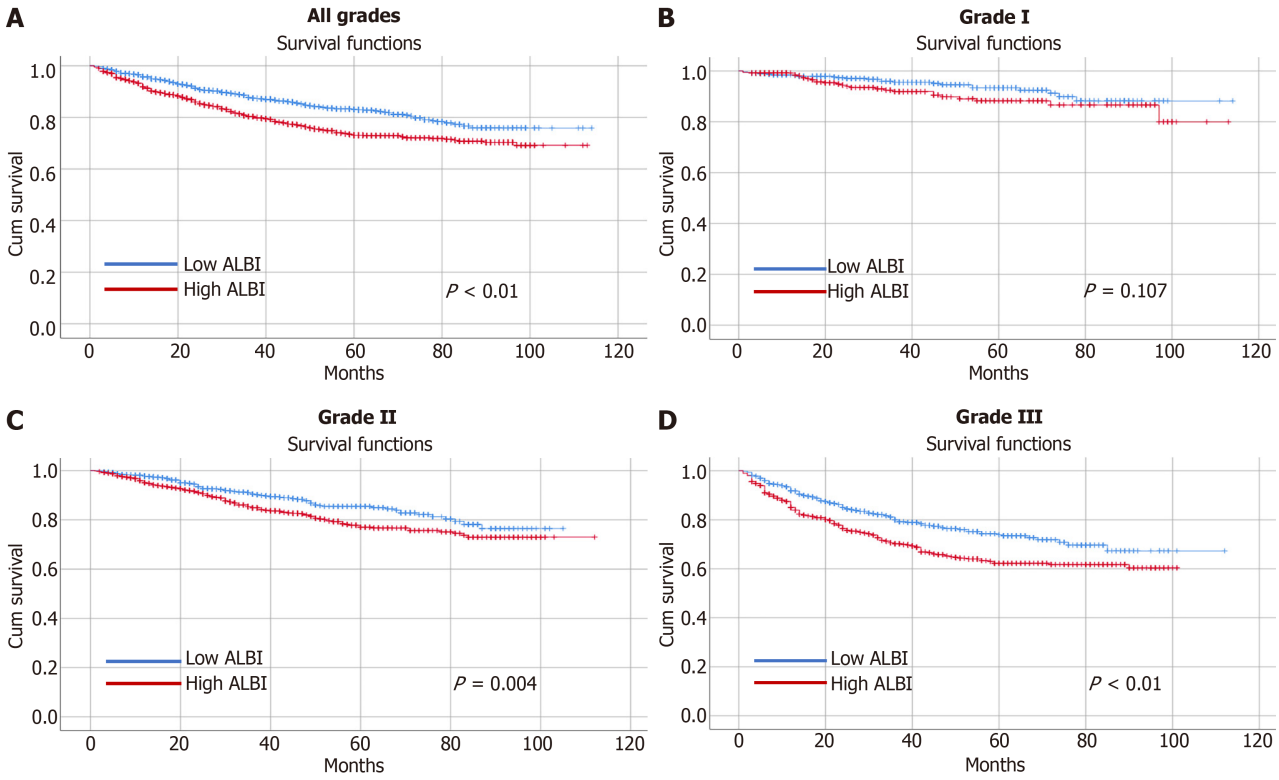

Figure 3 Kaplan-Meier survival curve analysis for impact of preoperative albumin-bilirubin score on disease-free survival of patients in all tumor-node-metastasis stages, stage I, stage II, and stage III. A: All tumor-node-metastasis stages; B: Stage I; C: Stage II; D: Stage III. ALBI: Albumin-bilirubin.

prognosis of metastatic CRC patients treated with regorafenib was shown in another retrospective study[29]. However, this group did not focus on CRC patients who underwent radical surgery. Zhu *et al*[26] first demonstrated that a high preoperative ALBI score was an independent indicator for both postoperative complications (38.2% *vs* 17.6%, $P < 0.001$) and OS (mean survival time, 47.6 mo *vs* 54.3 mo, $P = 0.005$) in 284 patients after radical surgery, and Koh *et al*[27] drew the same conclusion on OS (5-years OS, 86% *vs* 61.5%, $P = 0.002$). In our study, we found more postoperative complications in the high ALBI group, and the ALBI score was identified as an independent risk factor for OS, which was in accordance with the results of previous studies. The detailed information of the previous four studies is shown in Table 5.

We analyzed the impact of the preoperative ALBI score on OS and DFS of patients with tumors at different stages and found that the high ALBI group had worse OS and DFS for tumors at all stages, especially at stage II and stage III, than the low ALBI group. The results above indicated that even in patients who should have a good prognosis according to the TNM stage, the prognostic value of the ALBI score cannot be ignored. Although Zhu *et al*[26] reported that only patients in TNM stage III had a worse OS in the high ALBI group (mean survival time, 42.7 mo *vs* 51.6 mo, $P = 0.036$), the difference might be caused by the limited sample size of their study.

The ALBI scoring system was established based on the serum levels of ALB and bilirubin, which is an objective and convenient method for estimating liver function[33]. Hypoalbuminemia significantly increases postoperative complications and worsens OS in CRC patients after surgery[34,35]. In addition, some studies also illustrated that elevated serum bilirubin was an independent risk factor for OS[36,37], which might help to explain the prognostic value of the ALBI score. Serum albumin levels are closely correlated with nutritional status, and malnutrition can lead to a delay in recovery, increase the risk of infection, and impair immunity[22,33,38], resulting in more postoperative complications. Impaired immunity also causes the immune escape of tumor cells, which accelerates tumor recurrence and metastasis [39]. Moreover, elevated serum bilirubin often indicates liver dysfunction, and the latter might discontinue chemotherapy, which further influences OS and DFS[27,40]. However, our understanding of the underlying mechanism remains insufficient, and more studies are needed to clarify this issue.

Compared with previous studies, the baseline information in our study is more comprehensive. Additionally, a relatively large sample size of 4025 patients was included in our study, which was helpful for reducing bias and obtaining more reliable conclusions. However, our study has several limitations. Because this was a retrospective study conducted in a single center in southern China, biases were inevitable, and whether the results could be applied to other regions remains to be confirmed. Accordingly, to explore the prognostic role of the ALBI score in CRC patients after radical surgery, further multicenter prospective studies are needed.

Table 5 Previous studies reporting the albumin-bilirubin score of colorectal cancer patients

Ref.	Year	Country	Sample size	High ALBI, *n* (%)	Patients	Outcomes
Zhu *et al*[26]	2020	China	284	165 (58.1)	CRC	ALBI score was an independent indicator for postoperative complications and OS after radical surgery
Koh *et al*[27]	2022	South Korea	1015	173 (17.0)	CRC	ALBI score was an independent risk factor for OS in patients after radical CRC patients
Abdel-Rahman[28]	2019	Canada	1434	648 (45.2)	mCRC	ALBI score was an independent risk factor for OS and progression-free survival in CRC patients with liver metastasis after chemotherapy
Watanabe *et al*[29]	2021	Japan	60	28 (46.7)	CRC	High-ALBI group had shorter OS, and was correlated with shorter time to treatment failure and liver dysfunction in CRC patients treated with regorafenib

CRC: Colorectal cancer; mCRC: Metastatic colorectal cancer; ALBI: Albumin-bilirubin; OS: Overall survival.

CONCLUSION

A high preoperative ALBI score is correlated with adverse short-term outcomes, and the ALBI score is an independent risk factor for OS and DFS in patients with CRC undergoing radical surgery. Surgeons should take measures to improve the ALBI score preoperatively. However, despite the large sample size, this was a single-center retrospective study. Multicenter prospective studies are needed in the future to confirm our findings.

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FOOTNOTES

Author contributions: Diao YH and Shu XP contributed to the data analysis; Cheng Y led the quality assessments; Diao YH wrote the original draft; Shu XP and Cheng Y revised the manuscript. The data was gathered by all the authors. All authors have agreed on the manuscript to be submitted, provided final approval of the version to be published, and agree to be responsible for all elements of the work. Diao YH and Shu XP contributed equally to this work.

Institutional review board statement: This study was reviewed and approved by the Ethics Committee of The First Affiliated Hospital of Chongqing Medical University.

Informed consent statement: This is a retrospective study, and the patients came from a teaching hospital of the First Affiliated Hospital of Chongqing Medical University. When we delivered the ethics application, we also delivered application for exemption of informed consent.

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ORCID number: Yu-Hang Diao 0009-0004-0639-2954; Xin-Peng Shu 0000-0003-0652-4772; Yong Cheng 0000-0002-0161-435X.

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