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ORIGINAL RESEARCH

Preoperative Albumin-Bilirubin Grade as a Prognostic Predictor in Colorectal Cancer Patients Who Undergo Radical Resection

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Purpose: The relationship between liver function and colorectal cancer without liver metastases has not been explored. Therefore, we investigated whether the preoperative albumin-bilirubin grade could predict the prognosis of patients with colorectal cancer (CRC) undergoing radical resection, and we designed a quantifiable predictive model.

Patients and Methods: We retrospectively analyzed data from 284 patients with CRC who underwent radical resection in the Second Affiliated Hospital of the Wenzhou Medical University between January 2011 and January 2016. Patients were divided in two groups according to the calculated cut-off: the high albumin-bilirubin (>-2.48) grade and low albumin-bilirubin (≤-2.48) grade group. Kaplan–Meier curves were constructed to compare the overall survival (OS) between the two groups. Univariate and multivariate analyses were performed to identify the independent risk factors for postoperative complications and OS.

Results: Patients with a high albumin-bilirubin grade (n = 165, 58.1%) had a higher rate of postoperative complications (38.2% versus 17.6%, P < 0.001), especially medical (19.4% versus 6.7%, P = 0.002) and severe complications (1.7% versus 7.3%, P = 0.032). They also had a shorter OS (mean survival time, 47.6 versus 54.3 months, P = 0.005), especially patients with tumor-node-metastasis stage III (42.7 months versus 51.6 months, P = 0.036). Age ≥ 70 years (odds ratio [OR] = 2.22, P = 0.003) and high albumin-bilirubin grade (OR = 2.71, P = 0.001) were independent risk factors for postoperative complications, while age ≥ 70 years (hazard ratio [HR] = 2.65, P < 0.001), high albumin-bilirubin grade (HR = 1.81, P = 0.033), tumor-node-metastasis stage II (HR = 13.83, P = 0.010) and III (HR = 23.66, P = 0.002) were independent risk factors of OS.

Conclusion: Preoperative albumin-bilirubin grade could predict postoperative complications (especially medical and severe complications) and OS in patients with CRC, especially in those with tumor-node-metastasis stage III.

Keywords: colorectal cancer, albumin-bilirubin, liver function, prognosis, postoperative complications

Introduction

Colorectal cancer (CRC) is a common gastrointestinal disease worldwide. Data released by the National Cancer Center in 2017 showed that CRC was the fifth most lethal and fourth most incident malignant tumor.[1] Approximately 1–2 million new patients are diagnosed with CRC and approximately 500,000 deaths occur yearly.[2]

Presently, surgical resection and systemic chemotherapy are still the most effective methods for the treatment of CRC. The prognosis of patients with CRC,

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which is significantly influenced by local recurrence and distant metastasis, is of great concern to both patients and clinicians.[3] Many studies regarding prognosis prediction in patients with CRC have been carried out. Many recent studies based on molecular biomarkers such as KRAS, NRAS, BRAF, HER2 amplification, and miRNAs have been conducted to guide the personalized treatment of colorectal cancer.[4] Blood test indexes such as serum inflammatory indexes, blood routine tests, and blood coagulation function have been used to predict the prognosis of patients with CRC.[5–7] However, there is presently no blood biochemical index which can be used in clinical practice to predict the postoperative prognosis of colorectal cancer objectively and accurately. There is evidence indicating that liver biomarkers have a prognostic significance in various clinical diseases of non-hepatic origin,[8–10] and liver function indicators have a predictive significance in cancer with a hepatic origin.[11] Therefore, we hypothesized that there was a potential association between liver function and CRC.

The Child-Pugh (C-P) grade is of1used to assess liver function. It comprises the plasma albumin (ALB) level, total bilirubin (TB) level, prothrombin prolongation time, ascites, and hepatic encephalopathy; however, ascites and hepatic encephalopathy are too subjective to meet the clinical requirements. ALB and TB levels, as indicators of liver function, can reflect the synthesis and metabolic function of the liver. ALB level is one of the major indices of the Royal Marsden Hospital (RMH) prognostic score (range 0–3), which is an effective scoring system for evaluating tumor prognosis.[12] ALB and TB levels are also used for clinical diagnosis and characterization of the extent of liver damage. Recently, the albumin-TB (ALBI) grade has been proposed as a new method to evaluate liver function.[13] It is based on the objective index of ALB and TB, and is simple, objective, and has discriminatory advantages as compared to the C-P grade. Many retrospective studies further confirmed that the ALBI grading system has a good predictive value in liver function evaluation and prognosis evaluation in hepatocellular carcinoma (HCC).[11,13–15] The ALBI grade was first used to predict the prognosis in HCC and was subsequently validated for patients with chronic liver disease.[16,17] Indeed, it was not designed for patients with CRC; however, a recent study showed that the ALBI grade had predictive value for the prognosis in colorectal cancer with liver metastases.[18] It seemed that the ALBI grade had a potential of predicting prognosis in other pathologies other than HCC.

We therefore aimed to investigate whether the ALBI grade can predict short-term and long-term prognoses in patients with CRC undergoing radical resection and to design a simple and quantifiable predictive model.

Patients and Methods

Patients

Patients who underwent CRC surgery in the Second Affiliated Hospital of the Wenzhou Medical University between January 2011 and January 2016 were retrospectively included in this study. The inclusion criteria were as follows: 1) complete medical records, 2) age ≥ 18 years, 3) underwent elective colectomy with curative intent, 4) had not received preoperative chemotherapy or radiotherapy, 5) postoperative pathological confirmation of CRC, and 6) no liver metastases.

The exclusion criteria were as follows: 1) received palliative or emergency surgery, 2) had a history of another malignancy, 3) received preoperative chemotherapy or radiotherapy, and 4) lost to follow-up in less than 2 years.

Data Collection

Data were retrospectively collected from the medical records in the hospital's database. The variables of interest were as follows: 1) preoperative demographic and clinical features including age, sex, body mass index (BMI), preoperative plasma ALB and TB concentration (last preoperative test result), preoperative comorbidity (using the Charlson comorbidity index),[19] preoperative anemia (hemoglobin concentration < 120 g/L for men and < 110 g/L for women), preoperative bleeding, preoperative obstruction, tumor location, and abdominal surgery history; 2) Postoperative clinicopathological characteristics including tumor-node-metastasis (TNM) stage (7th edition of the American Joint Committee on Cancer),[20] tumor differentiation, operation method (the conversion from laparoscopy to laparotomy was defined as laparotomy), postoperative complications (Clavien-Dindo classification grade ≥ II postoperative complications during hospital stay or within 30 days after surgery),[21] length of postoperative hospital stay, and costs.

Follow-Up

Within 30 postoperative days, we followed up patients for complications through telephone. Telephone or outpatient follow-up was then conducted every 3 months until 5 years or until the cut-off date in January 2020. At every outpatient follow-up, physical and laboratory examinations were performed. A computed tomography scan of the abdomen and thorax was performed every 6 months during the first 3 years, and every year for up to 5 years. Follow-up time intervals were calculated from the surgery date. The patient's survival status, time of death, and cause of death were recorded.

Grouping ALBI Grade

The formula for ALBI used was as follows: ($\log_{10}$bilirubin × 0.66) + (albumin × −0.085), where TB was in µmol/L and ALB concentration was in g/L.[13] X-tile software version 3.6.1 (Yale University, USA) was used to determine the optimal cut-off value for the ALBI grade according to the calculated value.[22] The optimal cut-off was −2.48. We then divided the patients into two groups according to the ALBI grade: the low ALBI grade (ALBI≤-2.48) group and high ALBI grade (ALBI>-2.48) group.

Data Analysis

Normally distributed data are expressed as mean (standard deviation) and non-normally distributed data are expressed as median (interquartile range). Categorical variables are expressed as the number of patients (percentage). The independent samples *t*-test or non-parametric test were used to analyze continuous data, and the chi-square test or Fisher's exact test were used to analyze categorical variables. Univariate and multivariate analyses of various clinicopathological factors were carried out using binary logistic regression analysis with postoperative complications as the dependent factor. Overall survival (OS) was calculated from the date of surgery to the date of death or last available follow-up and was estimated using the Kaplan–Meier method. The Log rank test was used to compare survival curves. Univariate analysis for OS was carried out using the Cox regression analysis. Significant clinicopathological factors (P < 0.05, two-sided) in the univariate analysis were included in the multivariate Cox proportional hazards model, and a backward stepwise selection was performed. All the tests were statistically significant at P < 0.05 (two-sided). A visual prediction model of short-term complications and long-term survival was established using R software (The R Foundation, Vienna, Austria), based on the respective independent risk factors; the consistency index (C-index) was calculated.[23] Other statistical analyses were performed using SPSS software for Windows (version 22.0 IBM Corp., Armonk, USA).

Results

Clinicopathological Characteristics of Patients

By the end of the follow-up in January 2020, 69 patients had died. The median follow-up period was 40 months. There were 357 patients with colorectal cancer included in our database at the beginning, and 305 were retained after preliminary screening. Subsequently, 21 patients who were lost to follow-up for less than 2 years were also excluded. Finally, we included 284 patients in this study (Figure 1). The clinicopathological features of patients with CRC are shown in Table 1. Based on the cut-off value calculated using the X-tile software program, 119 (41.9%) patients with CRC had a low ALBI grade while 165 (58.1%) patients had a high ALBI grade. Patients in the high ALBI grade group were older than those in the low ALBI grade group (P = 0.014) and had a greater likelihood of developing intestinal obstruction (P = 0.005). The high ALBI grade group had poorer tumor differentiation (P = 0.012) and higher probability of postoperative complications (P < 0.001) than the low ALBI grade group. There were no significant differences in sex, BMI, preoperative comorbidity, preoperative anemia, preoperative bleeding, tumor location, TNM stage, surgery method, abdominal surgery history, length of postoperative hospital stay, and costs between both groups.

Short-Term Postoperative Complications

As shown in Table 2, 84 (29.6%) patients had postoperative complications. Complication and severe complication rates were higher in the high ALBI grade group than in the low ALBI grade group (38.2% versus 17.6%, P < 0.001; 7.3% versus 1.7%, P = 0.032, respectively). Based on the classification of complications, the incidence of medical complications was significantly higher in the high ALBI grade group (19.4% versus 6.7%, P = 0.002); moreover, there was no significant difference in the surgical complication rate between both groups (high ALBI grade versus low ALBI grade, 18.8% versus 10.9%, P = 0.071).

Table 3 shows the results of univariate and multivariate analyses for postoperative complications. In univariate analysis, age ≥ 70 years (odds ratio [OR] 2.39, P = 0.001), high ALBI grade (OR 2.88, P<0.001), and low/non-differentiation (OR 2.30, P = 0.030) were associated with postoperative complications. Multivariate analysis indicated that age ≥ 70 years (OR 2.22, 95% confidence interval [CI]: 1.30–3.80, P = 0.003) and high ALBI grade

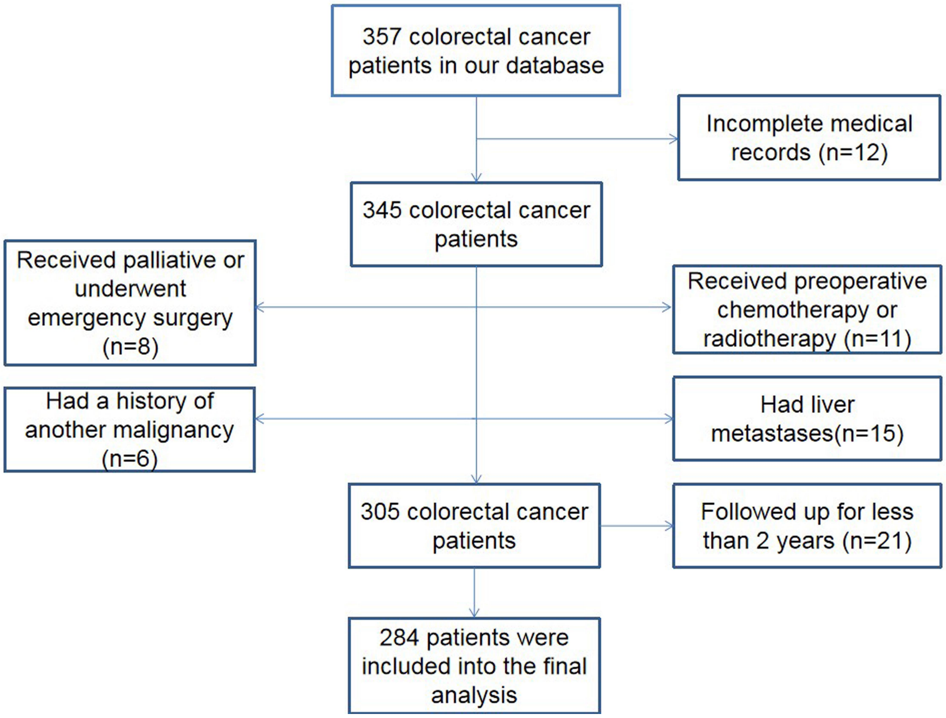

Figure 1 The patient screening flow chart.

(OR 2.71, 95% CI: 1.53–4.82, P = 0.001) were independent risk factors for postoperative complications.

Postoperative Overall Survival

As shown in Figure 2A, the high ALBI grade group had a shorter OS than the low ALBI grade group (mean survival time, 47.6 months versus 54.3 months, P = 0.005). When staging by TNM, we found no significant differences in OS between both groups in stage I and II (stage I, P = 0.344; stage II, P = 0.105), as shown in Figure 2B and C. In TNM stage III, the high ALBI grade group had a significantly worse OS than the low ALBI grade group [Figure 2D; mean survival time, 42.7 months versus 51.6 months, P = 0.036].

Univariate analysis demonstrated that age ≥ 70 years (HR 2.57, P < 0.001), high ALBI grade (HR 2.11, P = 0.007), Charlson comorbidity index ≥ 2 (HR 2.41, P = 0.010), preoperative anemia (HR 1.88, P = 0.035), preoperative obstruction (HR 2.56, P = 0.001), TNM stage (stage II, HR 15.47, P = 0.007; stage III, HR 22.17, P = 0.002), and low/non-differentiation (HR 2.45, P = 0.003) were associated with worse OS. In multivariate analysis, age ≥ 70 years (HR 2.65, 95% CI: 1.63–4.31, P < 0.001), high ALBI grade (HR 1.81, 95% CI: 1.05–3.11, P = 0.033), and TNM stage (stage II, HR 13.83, 95% CI: 1.88–102.06, P = 0.010; stage III, HR 23.66, 95% CI 3.25–172.06, P = 0.002) were identified as independent risk factors for OS (Table 4).

Visual Prediction Model of Postoperative Complications and Survival

Based on the independent risk factors of postoperative complications and OS, we created two nomograms to predict postoperative short-term outcomes and long-term outcomes (Figure 3). The nomogram that predicted postoperative complications is shown in Figure 3A; the prediction accuracy of this model was 66.6%. The visual prognosis prediction model for calculating the three-year and five-year survival rates according to the score of each index is shown in Figure 3B, and the C-index was 0.745.

Discussion

Preoperative ALBI grade, as a new method to assess liver function, has been validated in many retrospective studies.[13,24] Several studies have shown that the preoperative ALBI grade could predict prognosis in HCC.[14,15] Out of the sphere of HCC, a study also showed that the ALBI grade had a great predictive value in the prognosis of patients with CRC with liver metastases.[18] However,

Table 1 Clinicopathological Characteristics According to Albumin-Bilirubin (ALBI) Grade

Factors	Total (n=284)	Low ALBI Grade (n=119)	High ALBI Grade (n=165)	*P* value
Age,median (IQR),years	66 (17.75)	63 (18.00)	67 (18.00)	0.014*
Sex				0.788
Female	110 (38.7%)	45 (37.8%)	65 (39.4%)	
Male	174 (61.3%)	74 (62.2%)	100 (60.6%)	
BMI,mean (SD),kg/m^2	22.42 (3.07)	22.55 (3.17)	22.43 (3.34)	0.759
Preoperative ALB,median (IQR),g/L	38.55 (5.78)	41.60 (4.00)	35.80 (4.95)	<0.001*
Preoperative TB,median (IQR)μmol/L	10.65 (6.72)	9.20 (6.00)	11.70(6.95)	0.001*
Charlson comorbidity index				0.448
0	30(10.6%)	13(10.9%)	17(10.3%)	
1	46(16.2%)	23(19.3%)	23(13.9%)	
≥2	208(73.2%)	83(69.7%)	125(75.8%)	
Preoperative anemia				0.229
No	250(88.0%)	108(90.8%)	142(86.1%)	
Yes	34(12.0%)	11(9.2%)	23(13.9%)	
Preoperative bleeding				0.116
No	118(41.5%)	43(36.1%)	75(45.5%)	
Yes	166 (58.5%)	76 (63.9%)	90 (54.5%)	
Preoperative obstruction				0.005*
No	243 (85.6%)	110 (92.4%)	133 (80.6%)	
Yes	41 (14.4%)	9 (7.6%)	32 (19.4%)	
Tumor location				0.435
Colon	139 (48.9%)	55 (46.2%)	84 (50.9%)	
Rectum	145 (51.1%)	64 (53.8%)	81 (49.1%)	
TNM stage				0.436
I	55 (19.4%)	26 (21.8%)	29 (17.6%)	
II	102 (35.9%)	38 (31.9%)	64 (38.8%)	
III	127 (44.7%)	55 (46.2%)	72 (43.6%)	
Tumor differentiation				0.012*
High/Middle differentiation	238 (83.8%)	105 (88.2%)	133 (80.6%)	
Low/Non differentiation	32 (11.3%)	6 (5.0%)	26 (15.8%)	
Mucoid adenocarcinoma	14 (4.9%)	8 (6.7%)	6 (3.6%)	
Laparoscopic surgery				0.945
No	213 (75.0%)	89 (74.8%)	124 (75.2%)	
Yes	71 (25.0%)	30 (25.2%)	41 (24.8%)	
Abdominal surgery history				0.588
No	242 (85.2%)	103 (86.6%)	139(84.2%)	
Yes	42 (14.8%)	16 (13.4%)	26 (15.8%)	
Postoperative complications				<0.001*
No	200 (70.4%)	98 (82.4%)	102 (61.8%)	
Yes	84(29.6%)	21(17.6%)	63(38.2%)	
Postoperative hospital stays, median (IQR),days	16 (6.0)	15 (6.0)	16 (6.0)	0.268
Costs,median (IQR),¥	52,672 (21,798)	50,055 (19,503)	53,764 (24,580)	0.256

Note: *Statistically significant ($P < 0.05$).
Abbreviations: ALBI, albumin-bilirubin; IQR, interquartile range; BMI, body mass index; SD, standard deviation; ALB, albumin; TB, total bilirubin; TNM, tumor-node-metastasis.

Table 2 Patients' Postoperative Complications

Factors	Total (n=284)	Low ALBI Grade (n=119)	High ALBI Grade (n=165)	*P* value
Total complications	84 (29.6%)	21 (17.6%)	63 (38.2%)	<0.001*
Severe complications[a]	14 (4.9%)	2 (1.7%)	12 (7.3%)	0.032*
Classification of complications				
Surgical complications	44 (15.5%)	13 (10.9%)	31 (18.8%)	0.071
Gastrointestinal dysfunction[b]	8 (2.8%)	1 (0.8%)	7 (4.2%)	
Wound infection	14 (4.9%)	3 (2.5%)	11 (6.7%)	
Bleeding	1 (0.4%)	0 (0)	1 (0.6%)	
Intra-abdominal abscess	7 (2.5%)	3 (2.5%)	4 (2.4%)	
Anastomotic leakage	10 (3.5%)	5 (4.2%)	5 (3.0%)	
Intestinal obstruction	3 (1.1%)	1 (0.8%)	2 (1.2%)	
Urinary retention	1 (0.4%)	0 (0)	1 (0.6%)	
Medical complications	40 (14.1%)	8 (6.7%)	32 (19.4%)	0.002*
Pulmonary infection	13 (4.6%)	4 (3.4%)	9 (5.5%)	
Cardiac complications	3 (1.1%)	0 (0)	3 (1.8%)	
Venous thrombosis	3 (1.1%)	1 (0.8%)	2 (1.2%)	
Urinary infection	4 (1.4%)	0 (0)	4 (2.4%)	
Fever of unknown origin	4 (1.4%)	0 (0)	4 (2.4%)	
Transfusion[c]	9 (3.5%)	2 (1.7%)	7 (4.2%)	
Stroke	2 (0.7%)	1 (0.8%)	1 (0.6%)	
Mortality	2 (0.7%)	0 (0)	2 (1.2%)	

Notes: [a]Clavien-Dindo grade ≥ III; [b]Including prolonged postoperative diarrhea and constipation; [c]Including albumin and/or erythrocyte; *Statistically significant ($P < 0.05$).
Abbreviation: ALBI, albumin-bilirubin.

whether the preoperative ALBI grade can affect the prognosis of such patients without liver metastases has not been studied.

In this study, we calculated the ALBI score from previous HCC studies in which the ALBI grade cut-off values were −2.60 and −1.39.[11,13] However, these values were calculated preoperatively for patients with HCC and were obviously unsuitable for CRC. We then developed a new cut-off value of −2.48 from our dataset.

Using this criterion, we divided the patients into two groups: the high and low ALBI grade group (58.1% and 41.9%, respectively). We found a significant relationship between the ALBI grade and postoperative complications, and between the ALBI grade and long-term survival. A high ALBI grade was an independent risk factor of complications and OS. The high ALBI grade group had a significantly increased risk of medical and severe complications, but no risk of surgical complications. The possible mechanisms could be explained as follows. In view of the anatomical location and special structure of the liver, it has a large number of immune cells and can be seen as part of the immune system involved in adaptive and non-specific inflammatory responses.[25] An abnormal preoperative liver function may lead to an alteration in the systemic immunity and inflammation, coupled with interference of the tumor with various systems of the body. This will trigger a series of reactions and lead to a poor prognosis in patients with CRC. In addition, the lesions of liver functions affect the nutritional and metabolic state of the body, leading to a poor prognosis. Undoubtedly, the mechanism by which ALBI affects the prognosis of patients with colorectal cancer needs to be explained through further research. Previous studies have found that ALB and TB are reliable prognostic factors affecting the OS of cancer patients.[18,26] This finding was consistent with our results. We further analyzed the influence of the ALBI grade on OS in different TNM stages, and we found that a high ALBI grade had a significant effect on the OS of patients with TNM stage III CRC. This is mainly because patients with TNM stage I and II CRC had a good long-term prognosis. There was no significant association between ALBI grade and surgical complications in our study. This may be because surgical complications are mainly caused by surgical procedures and have little effect on the ALBI grade. The occurrence of medical and severe complications was more likely to be related to the patient's basic physical condition. Moreover, some studies have shown that decreased albumin levels are

Table 3 Results of Univariate and Multivariate Analyses of Risk Factors for Postoperative Complications

Factors	Univariate Analysis		Multivariate Analysis	
	OR (95% CI)	***P* value**	**OR (95% CI)**	***P* value**
Age,years				
<70	Reference		Reference	
≥70	2.39 (1.42–4.03)	0.001*	2.22 (1.30–3.80)	0.003*
Sex				
Female	Reference			
Male	0.90 (0.54–1.52)	0.696		
ALBI grade				
Low ALBI grade	Reference		Reference	
High ALBI grade	2.88 (1.64–5.08)	<0.001*	2.71 (1.53–4.82)	0.001*
BMI				
<18.5	1.82 (0.81–4.08)	0.145		
18.5–24	Reference			
>24	1.25 (0.71–2.21)	0.441		
Charlson comorbidity index				
<2	Reference			
≥2	1.50 (0.82–2.74)	0.190		
Preoperative anemia				
No	Reference			
Yes	1.56 (0.74–3.29)	0.241		
Preoperative bleeding				
No	Reference			
Yes	0.81 (0.48–1.35)	0.414		
Preoperative obstruction				
No	Reference			
Yes	1.28 (0.64–2.59)	0.489		
Tumor location				
Colon	Reference			
Rectum	1.08 (0.65–1.80)	0.772		
TNM stage				
I	Reference			
II	1.53 (0.74–3.18)	0.255		
III	1.11 (0.54–2.29)	0.769		
Tumor differentiation				
High/Middle differentiation	Reference			
Low/Non differentiation	2.30 (1.09–4.87)	0.030*		
Mucoid adenocarcinoma	0.71 (0.19–2.63)	0.609		
Laparoscopic surgery				
No	Reference			
Yes	0.5 (0.30–1.06)	0.074		
Abdominal surgery history				
No	Reference			
Yes	1.08 (0.53–2.20)	0.833		

Notes: Univariate analysis showed that the clinicopathological factors with P<0.05 were included in the multivariate analysis (backward stepwise selection: LR); *Statistically significant (P < 0.05).

Abbreviations: OR, odds ratio; CI, confidence interval; ALBI, albumin-bilirubin; BMI, body mass index; TNM, tumor-node-metastasis.

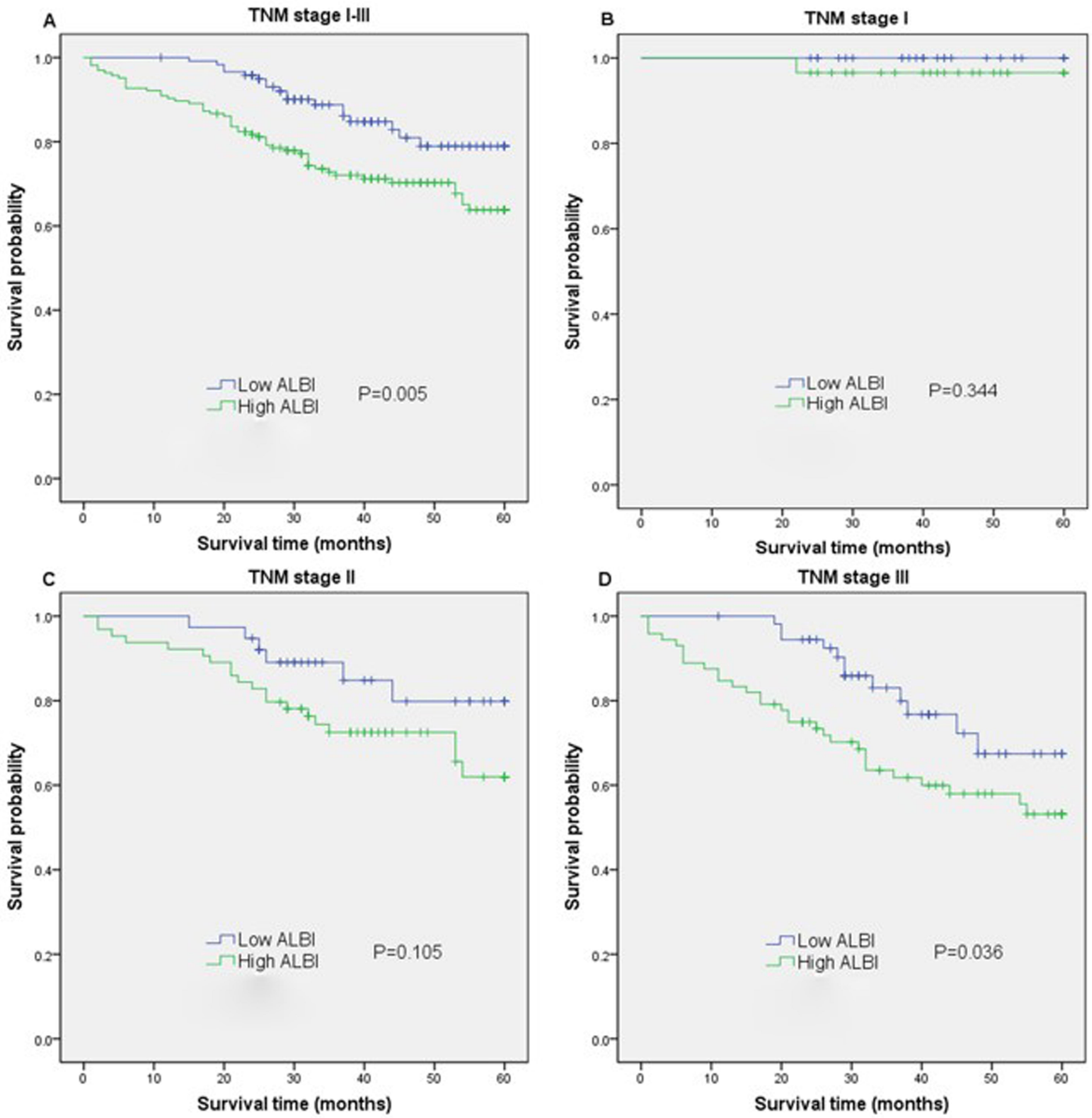

Figure 2 Kaplan–Meier curves for comparing overall survival between the high ALBI grade group and the low ALBI grade group with different TNM stages. Survival curves for (**A**) patients with TNM stage I–III; (**B**) patients with TNM stage I; (**C**) patients with TNM stage II; (**D**) patients with TNM stage III.
Abbreviations: ALBI, albumin-bilirubin; TNM, tumor-node-metastasis.

associated with serious complications.[27,28] This is suggestive that an abnormal liver function could lead to an increased risk of postoperative complications. We also found that the ALBI grade had a better predictive ability for OS than for postoperative complications of CRC (C-index 0.745 versus 0.666).

We found that age ≥ 70 years was an independent risk factor for the prognosis of patients with CRC. This was consistent with the findings of a previous study.[2] The mortality rate due to CRC increases with age. According to an epidemiological survey in China, the mortality rate of patients with CRC aged over 70 years was more than 60%.[29] Body functions and the ability to repair surgical trauma weaken with age. Therefore, it is predictable that advanced age is an independent risk factor for postoperative complications.

Table 4 Results of Univariate and Multivariate Analyses of Risk Factors for Overall Survival

Factors	**Univariate Analysis**		**Multivariate Analysis**	
	HR (95% CI)	***P* value**	**HR (95% CI)**	***P* value**
Age,years				
<70	Reference		Reference	
≥70	2.57 (1.60–4.14)	<0.001*	2.65 (1.63–4.31)	<0.001*
Sex				
Male	Reference			
Female	1.20 (0.75–1.94)	0.446		
ALBI grade				
Low ALBI grade	Reference		Reference	
High ALBI grade	2.11 (1.23–3.61)	0.007*	1.81 (1.05–3.11)	0.033*
BMI				
<18.5	0.82 (0.37–1.82)	0.624		
18.5–24	Reference			
>24	0.66 (0.37–1.16)	0.149		
Charlson comorbidity index				
<2	Reference			
≥2	2.41 (1.23–4.72)	0.010*		
Preoperative anemia				
No	Reference			
Yes	1.88 (1.05–3.39)	0.035*		
Preoperative bleeding				
No	Reference			
Yes	0.74 (0.46–1.19)	0.215		
Preoperative obstruction				
No	Reference			
Yes	2.56 (1.49–4.40)	0.001*		
Tumor location				
Colon	Reference			
Rectum	0.76 (0.47–1.21)	0.246		
TNM stage				
I	Reference		Reference	
II	15.47 (2.10–114.04)	0.007*	13.83 (1.88–102.06)	0.010*
III	22.17 (3.05–161.12)	0.002*	23.66 (3.25–172.06)	0.002*
Tumor differentiation				
High/Middle differentiation	Reference			
Low/Non differentiation	2.45 (1.35–4.43)	0.003*		
Mucoid adenocarcinoma	2.10 (0.84–5.28)	0.114		
Laparoscopic surgery				
No	Reference			
Yes	0.74 (0.40–1.35)	0.324		
Abdominal surgery history				
No	Reference			
Yes	1.37 (0.73–2.55)	0.327		

Notes: Univariate analysis showed that the clinicopathological factors with P<0.05 were included in the multivariate analysis (backward stepwise selection: LR); *Statistically significant (P < 0.05).
Abbreviations: HR, hazard ratio; CI, confidence interval; ALBI, albumin-bilirubin; BMI, body mass index; TNM, tumor-node-metastasis.

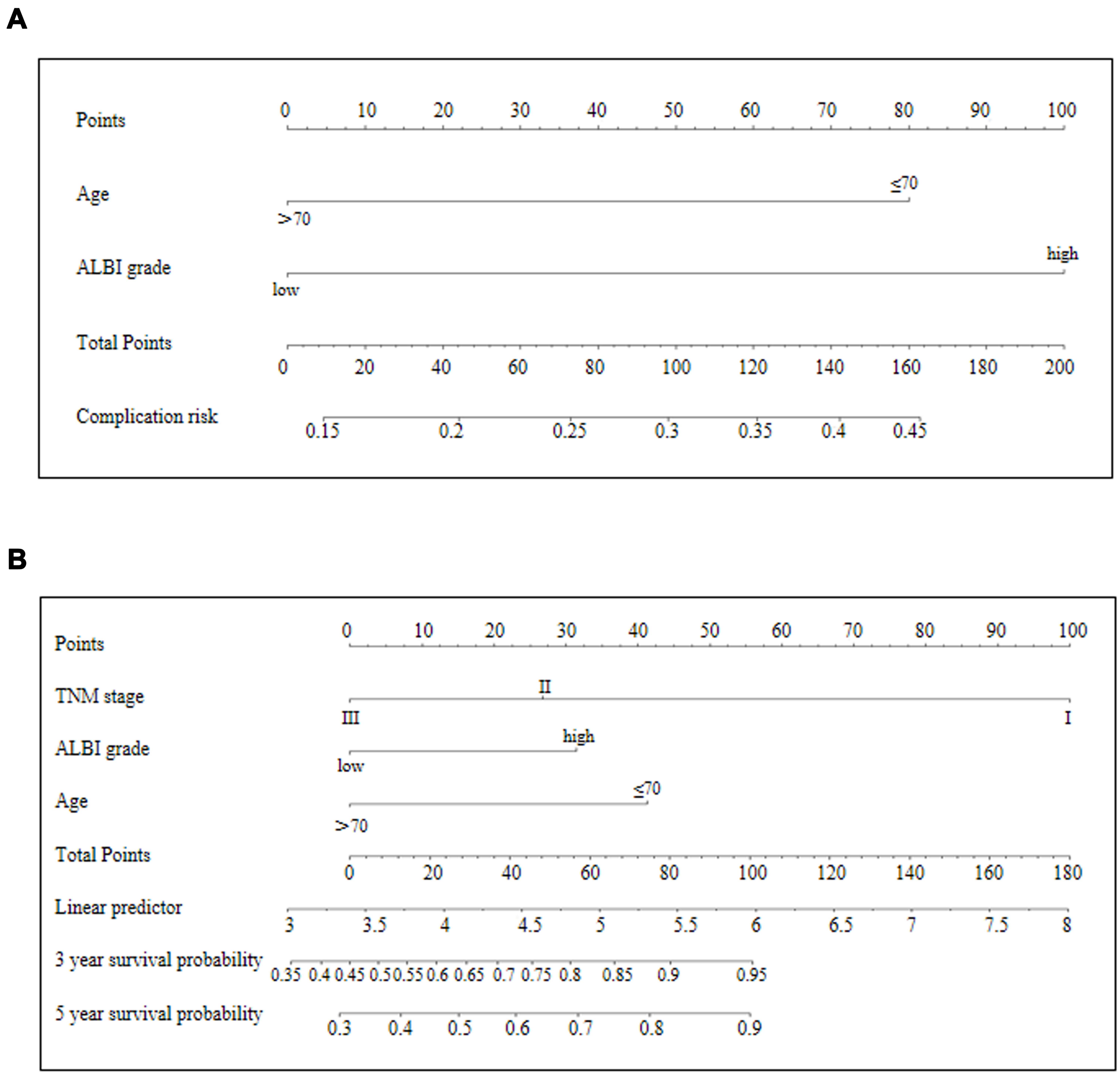

Figure 3 (**A**) Nomogram for postoperative complications; (**B**) Nomogram for postoperative survival.
Abbreviations: ALBI, albumin-bilirubin; TNM, tumor-node-metastasis.

To our knowledge, this is the first study to report on the relationship between preoperative ALBI grade and CRC without liver metastases. As expected, we found that preoperative ALBI grade had a distinct significance in CRC prognosis. ALBI grade has the advantages of preoperative availability, simplicity, and objectivity. This could be a useful tool for surgeons for preoperative prognosis prediction and postoperative clinical decision making in patients with CRC. Our subsequent study will focus on preoperative intervention in patients with CRC with a high ALBI grade to investigate whether preoperative intervention can improve patient prognosis.

Our study had several limitations. First, the predictive model of the ALBI grade showed a good predictive ability in the survival analysis of only patients with TNM stage III, since those with stage I and II had a high postoperative survival rate. This can be accounted for in further studies by using a larger sample size for all TNM stages to perfect the ALBI grade predictive model. The ALBI model's efficiency in predicting postoperative complications was also inadequate. This requires a larger sample size including more predictive factors to improve it. Second, this was a single-center retrospective study. The conclusions of this study need to be verified in future multicenter prospective studies. It would also be interesting to be performed comparison of the conclusions of this study, in view of different geographical areas (Chinese vs non-Chinese population).

Conclusion

The preoperative ALBI grade could predict postoperative complications (especially medical and severe complications) and OS in patients with CRC, especially in patients with TNM stage III CRC. Age ≥ 70 years and high ALBI grade were independent risk factors for postoperative complications, while age ≥ 70 years, high ALBI grade, and TNM stage II and III were independent risk factors for OS. The ALBI grade prediction model had better accuracy in predicting long-term survival than short-term complications of CRC. In addition, preoperative assessment of the ALBI grade could provide a new approach for predicting the prognosis of patients with CRC and for guiding surgeons for better preoperative preparation.

Data Sharing Statement

The data of this study are available from the corresponding author on reasonable request.

Ethics Approval and Informed Consent

This study was carried out in accordance with the guidelines stipulated in the Declaration of Helsinki. All patients provided written informed consent. This study was approved by the Ethics Committee of the Second Affiliated Hospital of Wenzhou Medical University.

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Disclosure

The authors report no conflicts of interest in this work.

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