

Preoperative carcinoembryonic antigen to body mass index ratio contributes to prognosis prediction in colorectal cancer

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Abstract. Both carcinoembryonic antigen (CEA) level and body mass index (BMI) are traditional prognostic markers in colorectal cancer (CRC); however, to the best of our knowledge, the value of the CEA to BMI ratio (CBR) has never been addressed. In the present study, 191 patients with CRC treated using radical resection were retrospectively included, and the significance of the CBR in predicting disease-free survival (DFS) or overall survival (OS) rates was calculated. The prognostic efficacy of the CBR in predicting OS was compared with individual CEA and BMI values. The survival differences of the subgroups were calculated by Kaplan-Meier analysis, and corresponding risk factors were then estimated by a Cox proportional hazards model. As a result, 29.84% (57/191) of the patients were assigned to the high CBR group (cut-off, ≥ 0.28); the CBR had a sensitivity of 56.50 and 68.90%, and a specificity of 80.60 and 80.10% for DFS and OS, respectively. Patients with a high CBR more commonly underwent laparotomy and exhibited advanced T stages, the presence of tumor deposits and advanced Tumor-Node-Metastasis stages (stage II or III). The CBR was more efficient than the CEA or BMI alone in predicting OS. In addition, patients with a high CBR presented with a significantly worse outcome than patients with a low CBR. Finally, the CBR was an independent risk factor for both DFS and OS. In conclusion, the CBR was a more robust prognostic factor in CRC, and patients with a relatively high CBR exhibited poorer survival.

Introduction

Colorectal cancer (CRC) remains a life-threatening disease worldwide (1), with an incidence rate that increases annually by ~2% and a death rate that increases annually by ~1.3% among those <50 years of age (2). In recent years, a group of prognostic markers obtained from patients' routine blood tests, such as the neutrophil to lymphocyte ratio (NLR) (3) and the lymphocyte to monocyte ratio (LMR) (4), have been established. These indicators are non-invasive and easily accessible in practice; however, their prognostic efficacies have not been conventionally compared with traditional markers.

Body mass index (BMI), which is calculated as weight in kilograms divided by height in meters squared (kg/m^2), is a traditional prognostic marker for numerous malignancies, including breast (5), ovarian (6), esophageal (7), lung (8) and gastric (9) cancer, as well as CRC (10-12). However, there are still unresolved problems regarding the prognostic value of BMI in CRC. On the one hand, the BMI criteria to group patients have been inconsistent in previous studies; for example, Guercio *et al* (13) divided patients into 5 subgroups [<21 (underweight), 21-24.9 (normal), 25-29.9, 30-34.9 and 35 kg/m^2], as did Chiu *et al* (11); however, in the latter study, underweight ($<18.50 \text{ kg}/\text{m}^2$) and normal weight (18.50-24.99 kg/m^2) patients were not in line with those in the former study. Furthermore, Song *et al* found that 20.2 kg/m^2 was the best discrimination point for survival (12). In addition, the final conclusion for the role of BMI in CRC is conflicting, with some studies indicating that patients with an underweight BMI ($<18.50 \text{ kg}/\text{m}^2$) would have poor survival (10-12), but other studies failing to reproduce these results (13) or even yielding opposite results (14). Based on this background, it is reasonable to improve the prognostic efficacy of BMI with a combination of other markers. In fact, other studies have tried to combine BMI with other markers, including the NLR (15,16); however, these studies did not routinely report the prognostic efficacy of the new indicators or statistically compare them when it was generated.

The carcinoembryonic antigen (CEA) level is another long-term established tumor marker that is recommended by the American Society of Clinical Oncology for CRC (17) and has been incorporated into the Tumor-Node-Metastasis (TNM) system (the so-called C-stage) to provide additional prognostic information (18). However, apart from the fact that

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only 21-36% of patients are positive for CEA at diagnosis (19), limitations such as a low sensitivity of a single CEA value for prognosis cannot be ignored (20), and its efficacy could be largely attenuated in conditions such as type II diabetes (21) or smoking (22). Notably, in previous studies, the serum concentration of CEA was closely correlated with BMI; for example, an increase or decrease in BMI in patients with cancer was correlated with a fluctuation in systemic inflammatory factors such as interleukin-6 (IL-6) (23,24), which can promote the secretion of CEA in CRC cells (25,26). Based on these factors, it is reasonable to explore the prognostic value of the CEA to BMI ratio (CBR) in CRC, as the significance of CEA levels could be balanced to some extent by BMI in these patients; however, to the best of our knowledge, associated reports are still absent.

The present study aimed to explore the prognostic value of the CBR, as well as its prognostic efficacy when compared with individual CEA, BMI and other inflammatory prognostic indicators in CRC.

Materials and methods

Patients. Between January 2012 and October 2021, patients with CRC who underwent radical resection of primary lesions at Hainan Hospital of Chinese People's Liberation Army (PLA) General Hospital (Sanya, China) were retrospectively included in the present study. Patients meeting any one of the following criteria were excluded: i) Patients with an absence of preoperative laboratory test results or abnormal aminotransferase or serum creatinine levels, since such abnormalities could cause an altered metabolism or excretion of CEA (27,28); ii) patients with distant lesions; iii) patients who were missing any TNM information in their postoperative pathological reports; iv) patients with multiple or recurrent malignancies or *in situ* lesions; v) and patients with a follow-up time of <36 months. In addition, patients who received neoadjuvant chemotherapy were also excluded, since such therapy could cause problems in being able to accurately confirm the pT/pN stages in post-operative pathological findings, in particular for those who reached a tumor regression grading of 2 or 3 (29). A binary system was applied for patients with cancer with or without mucinous elements, tumor deposits (TDs) and risk factors (with perineural or lymphovascular invasion). Other clinicopathological parameters were recorded as described in previous studies (30,31). The study was performed in line with the principles stated in the Declaration of Helsinki and was approved by the Ethics Committee of Hainan Hospital of Chinese PLA General Hospital (approval no. 301HLFYLS15). All patients or their authorized relatives provided written informed consent.

Determination of the CBR, NLR, LMR, platelet to lymphocyte ratio (PLR) and prognostic nutritional index (PNI), and their correlations. Laboratory tests were performed as described in our previous studies (30,31). The CBR was calculated as the concentration of serum CEA (reference, 0-5 $\mu\text{g/ml}$) divided by the BMI. In addition, other inflammatory prognostic indicators, including NLR, LMR, PLR and PNI, were also determined according to previous studies (3,4,32,33). The correlation of CBR with NLR, LMR, PLR and PNI was also determined.

Definitions of disease-free survival (DFS) and overall survival (OS). The follow-up was conducted as previously described (31). Briefly, patients were interviewed every 3-6 months for the first 2 years and then every 6-12 months after for those who survived for >2 years. DFS time was defined as the time from the date of surgery until the date of the first recurrence or metastasis at any location, or death from any reason. OS time was defined from the same initial point to the date of death from any cause. The latest follow-up point was December 2021.

Statistical analysis. Statistical analyses were conducted using SPSS 20.0 (IBM Corp.) and MedCalc v19.0.7 (MedCalc Software bvba). The optimal discriminator point of the CBR was calculated by receiver operating characteristic (ROC) curve analysis, and then the area under the curve (AUC) was compared using the methods described by DeLong *et al* (34). The differences in the clinicopathological parameters between the CBR subgroups were estimated by χ^2 test. The association of CBR with other inflammatory prognostic indicators was determined by Pearson's correlation analysis. Survival differences for the low or high CBR subgroups were determined by Kaplan-Meier analysis followed by log-rank tests. A Cox proportional hazards model was applied to select the risk factors for survival (forward likelihood ratio model). Based on the results of the multivariable analysis, nomograms were established using R (version 4.1.1; <http://www.r-project.org>) with the survival and RMS package, and the C-index was used to determine the prediction efficacy. $P < 0.05$ (two-sided) was considered to indicate a statistically significant difference.

Results

Demographic features and the prognostic efficacy of the CBR. As shown in Fig. 1, a total of 191 patients (68 females and 123 males) were finally included in the study. The mean age of the patients was 59.3 years (range, 24-85 years), with a mean follow-up period of 51.1 months (range, 1-111 months). By ROC analysis, taking 0.28 as the optimal cutoff point (according to the Youden index), 29.84% (57/191) of the patients were assigned to the high CBR group (≥ 0.28), and 70.16% (134/191) were assigned to the low CBR group (< 0.28). The CBR presented a sensitivity of 56.50 and 68.90%, and a specificity of 80.60 and 80.10% for DFS and OS, respectively (both $P < 0.01$) (Fig. 2). Next, a further comparison of the prognostic efficacy of the CBR in predicting OS with individual CEA ($Z = 2.35$, $P = 0.02$), BMI ($Z = 2.01$, $P = 0.04$), NLR ($Z = 2.90$, $P < 0.01$), LMR ($Z = 2.42$, $P = 0.02$) and PLR ($Z = 2.49$, $P = 0.01$) values indicated significant differences, with the exception of PNI ($Z = 1.16$, $P = 0.25$).

Correlation of CBR with NLR, LMR, PLR and PNI. According to Pearson's correlation analysis, the CBR displayed a significant positive association with NLR ($r = 0.20$, $P = 0.01$) and PLR ($r = 0.21$, $P < 0.01$), whereas a negative association was exhibited with LMR ($r = -0.17$, $P = 0.02$) and PNI ($r = -0.20$, $P = 0.01$) (Fig. 3).

Clinicopathological parameter differences between the high- and low-CBR subgroups. According to the χ^2 test, patients

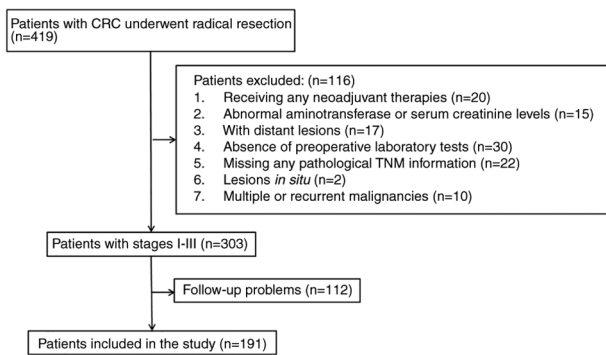


Figure 1. A consort diagram of the study. TNM, Tumor-Node-Metastasis; CRC, colorectal cancer.

who underwent a laparotomy ($P=0.03$), or those with advanced T stages (T_3+T_4) ($P<0.01$), the presence of TD(s) ($P<0.01$) and advanced TNM stages (stage II or III) ($P<0.01$) were more commonly found in the high CBR group. No significant differences were found for the other clinicopathological parameters between the high and low CBR subgroups (Table I).

Survival differences between the high and low CBR subgroups in terms of DFS and OS. After the 3-year follow-up period, significant differences in DFS (43.86 vs. 83.58%; $P<0.01$) and OS (56.14 vs. 89.55%; $P<0.01$) rates were found between the high and low CBR subgroups, respectively (Fig. 4A and B). Subsequently, the survival differences of the low and high CBR subgroups were further compared in different stages, and it was indicated that patients with a low CBR would have a superior DFS and OS in stage II (with a tendency but non-significant result for DFS) and stage III patients but not in stage I cases (Fig. 4).

Univariate and multivariate analyses of the prognostic factors for DFS and OS. Univariate tests indicated that type of resection, T, N and TNM stages, TDs, risk factors, pre-operative NLR, LMR, PLR, PNI and CBR were all factors that could affect DFS (Table II), and that these, in addition to histological grade and mucinous elements, were factors that could affect OS (Table III). When these significant factors (only those $P<0.05$) were included in the multivariate tests for DFS and OS, the results indicated that the TDs, PNI and CBR were independent prognostic factors for both DFS (CBR: HR, 3.48; 95% CI, 2.04-5.91; $P<0.01$) and OS (CBR: HR, 3.71; 95% CI, 1.95-7.08; $P<0.01$). Additionally, N stage was an independent prognostic factor for DFS, and histological grade, mucinous element and risk factors were independent prognostic factor for OS (Tables II and III).

Development of nomograms for predicting CRC prognosis. To predict DFS and OS rates for the patients, nomograms were constructed based on the multivariate analyses in Tables II and III. Each factor received a corresponding total point according to the nomograms. As shown in Fig. 5, the C-indexes for the prediction of 3-year DFS and OS were 0.81 (95% CI, 0.72-0.91) and 0.84 (95% CI, 0.71-0.96), respectively (Fig. 5A and B), which indicated that the model provided good discrimination. In addition, the calibration curves displayed a

good consistency between the predicted results and the actual results (Fig. 5C and D).

Discussion

The present study found that the CBR was significant in the prognosis of CRC, and that the prognostic efficacy of the CBR was superior to individual CEA, BMI, NLR, PLR and LMR values, with a relatively high sensitivity and specificity. Patients with a high CBR had a worse outcome than patients with a low CBR. Taking into consideration that the CBR was less likely to be influenced by common acute complications such as infection, bleeding and obstruction in CRC, it should be considered a robust prognostic indicator in practice. To the best of our knowledge, the present study is the first report concerning the value of the CBR in CRC.

Both CEA levels and BMI are traditional prognostic markers in CRC, but have individual limitations. In previous studies on CEA levels, the positive rate was relatively low (19), and although patients with a normal range of CEA also had prognostic significance based on reduced cutoff points (35,36), the sensitivity was relatively low (46.00%) (37) with a limited AUC in predicting survival that ranged from 0.636 (cutoff, 11 $\mu\text{g/ml}$) (38) and 0.645 (cutoff, 5 $\mu\text{g/ml}$) (39) to 0.740 (cutoff, 12.5 $\mu\text{g/ml}$) (40). A recent study indicated that the CEA to maximum tumor diameter ratio has prognostic value; however, the AUC of the new marker in predicting 3-year OS was reported to be only 0.704 (41). For BMI, its application in prognosis was largely blocked by inconsistent criteria and conflicting results, as aforementioned (10-14). Similarly, some reports indicated that combining BMI with other markers, such as lymphocyte counts, could improve the prognostic efficacy for patients with head and neck cancer who underwent radiation therapy (16). Recently, Xie *et al* (42) conducted a study that included 2,471 patients with CRC and found that the neutrophil-BMI ratio was a useful prognostic marker. In the present study, CBR presented with a relatively high sensitivity and specificity for OS. Furthermore, the prognostic efficacy was markedly stronger than that of individual CEA and BMI values, and even greater than NLR, LMR and PLR values.

Taking into consideration the individual role of CEA levels and BMI in CRC prognosis, these results could be explained from the following perspectives. First, for patients falling in a certain BMI range, a relatively high CEA (equal to a high CBR) would correlate with poor survival, which has been well established by previous clinical studies (35,43). Molecularly, it is well known that up to 90% of CRC cells can release CEA (44,45), and CEA can trigger CRC progression by inducing epithelial-mesenchymal transition, increasing cancer cell invasiveness and inhibiting apoptotic signaling (46). In addition, CEA can also cause radioresistance in CRC cells in the presence of M2 macrophages (47). Based on these facts, a high CBR weighted by a high CEA was likely to be associated with poor outcomes in the patients. Second, for those with a similar concentration of CEA, a lower BMI (also indicating a high CBR) would lead to worse outcomes, which was also in line with previous observations (10-12). However, it is also notable that certain studies indicated that a high BMI, particularly for class I (BMI, 30-35 kg/m^2) and II (BMI, $\geq 35 \text{ kg/m}^2$) obesity, was correlated with poor survival in CRC (48,49). In

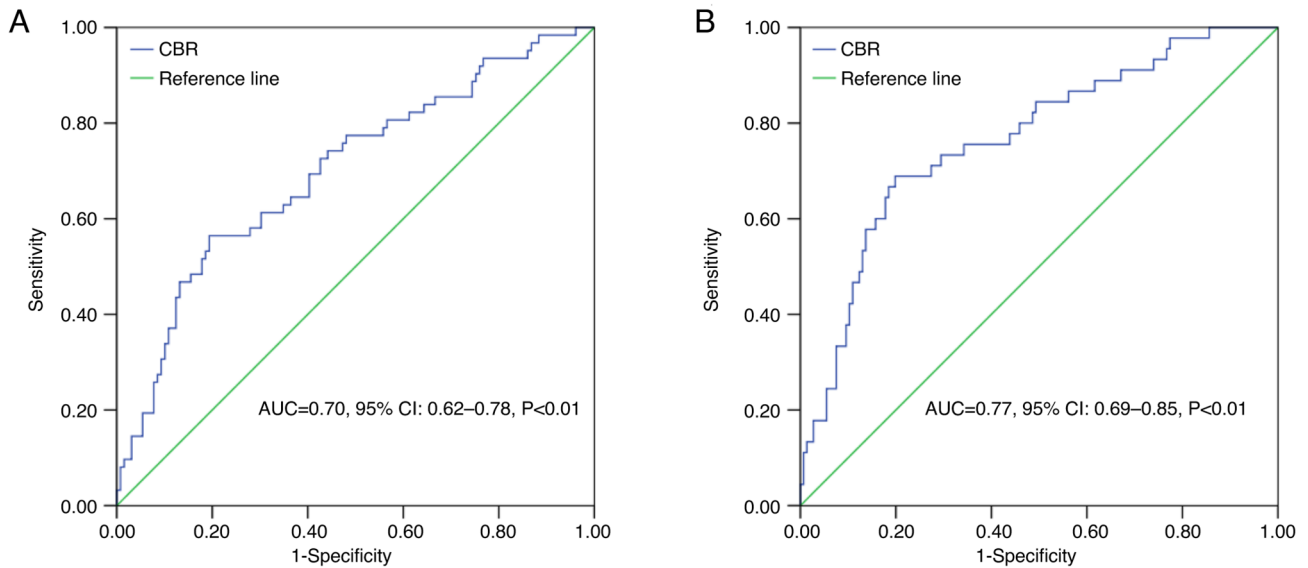


Figure 2. Receiver operating characteristic analysis of the CBR for (A) disease-free survival and (B) overall survival. AUC, area under the curve; CBR, carcinoembryonic antigen to body mass index ratio.

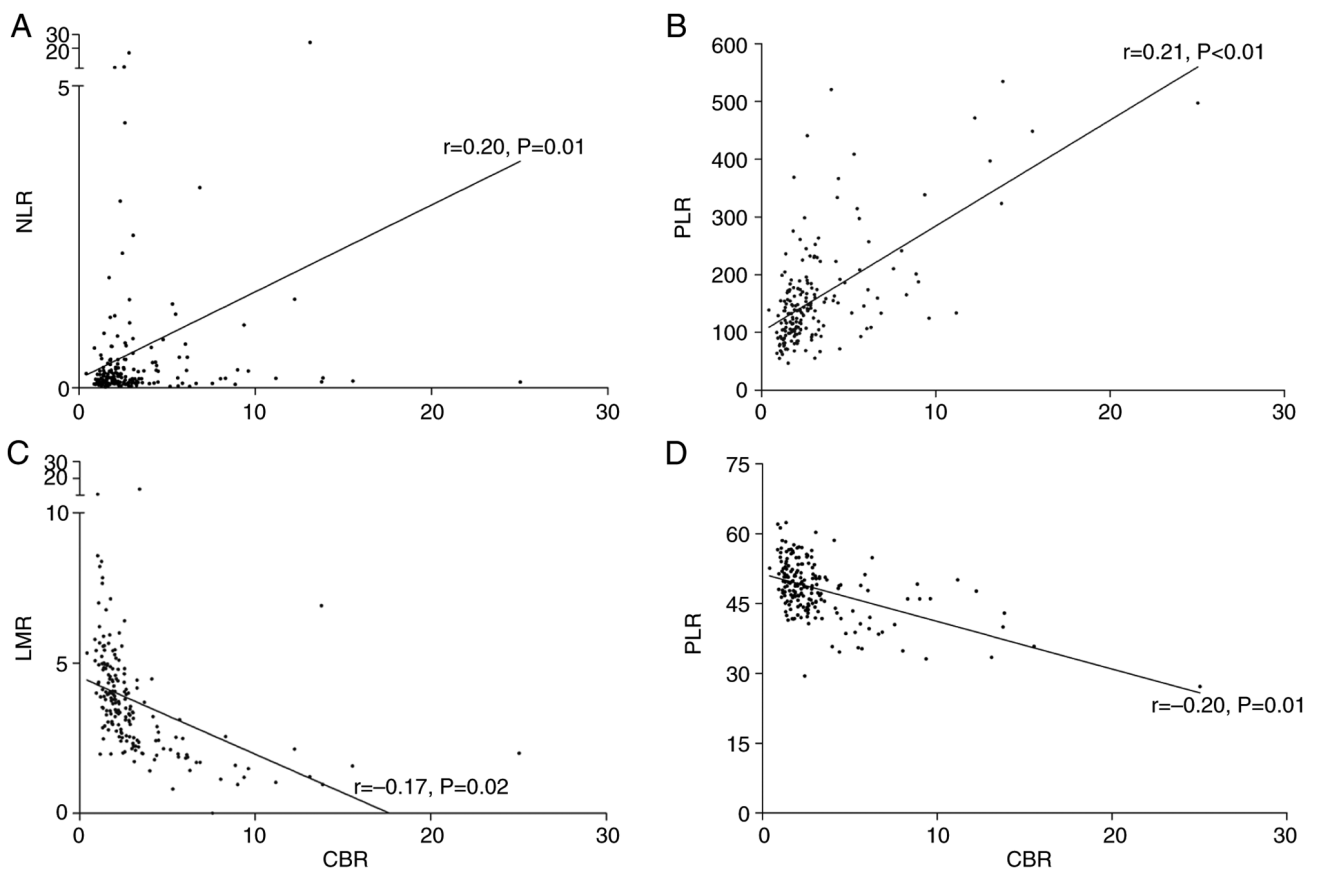


Figure 3. Correlation of CBR with other inflammatory prognostic indicators, including (A) NLR, (B) PLR, (C) LMR and (D) PNI. CBR, carcinoembryonic antigen to body mass index ratio; NLR, neutrophil to lymphocyte ratio; LMR, lymphocyte to monocyte ratio; PLR, platelet to lymphocyte ratio; PNI, prognostic nutritional index.

fact, previous studies found an increasing incidence of newly diagnosed liver disorder in obese patients (50), and a relationship between BMI and serum liver enzyme activity (51); subsequently, the metabolism or excretion of CEA was altered and had a tendency to be higher in patients with a high

BMI (27). However, studies concerning the CEA level in individuals with a high BMI, particularly in those with class I or class II obesity, are rare, and it is still largely unknown whether the CBR is also applicable in such a scenario (only 5 patients had a BMI of >30 in the present study).

Table I. Differences in clinicopathological parameters among CBR subgroups.

Characteristic	Total patients, n	CBR		P-value
		Low, n	High, n	
Age, years				0.35
<60	91	67	24	
≥60	100	67	33	
Sex				0.74
Female	68	49	19	
Male	123	85	38	
Type of resection				0.03 ^a
Laparotomy	29	15	14	
Laparoscopy	162	119	43	
Tumor location				0.25
Right	42	26	16	
Left	149	108	41	
Histological grade				0.38
Well + moderate	162	116	46	
Poor	29	18	11	
Mucinous element				0.16
Present	37	22	15	
Absent	154	112	42	
T stages				<0.01 ^a
T ₁ + T ₂	51	44	7	
T ₃ + T ₄	140	90	50	
N stages				0.11
N ₀	115	86	29	
N ₁ + N ₂	76	48	28	
Tumor deposits				<0.01 ^a
Present	171	126	45	
Absent	20	8	12	
TNM stages				<0.01 ^a
I	40	38	2	
II	75	48	27	
III	76	48	28	
Risk factors				0.09
Present	24	13	11	
Absent	167	121	46	

^aP<0.05. TNM, Tumor-Node-Metastasis; CBR, carcinoembryonic antigen to body mass index ratio.

Cancer-related inflammation has a profound effect in regulating cancer development and is regarded as a hallmark of it (52). High CBR associated with poor survival could be also understood from the perspective of inflammation. Previous studies indicated that CEA in patients with CRC could induce the secretion of IL-6, and that the levels of CEA and IL-6 were positively correlated (16,53). It was noted that IL-6 could induce fat loss in cancer cachexia via different approaches, such as promoting white adipose tissue lipolysis (54) and decreasing muscle mass (55), which could result in a decreased BMI in these patients (56). Based on these facts, it was

plausible that a high CBR indicated a high level of inflammation and a high tendency for reduced BMI, which could present as cachexia and poor survival. The present study also found that a high CBR was associated with advanced T stage (T₃+T₄), and the presence of TDs. CBD was positively associated with NLR or PLR and negatively associated with LMR or PNI on correlation analysis; in fact, these parameters were also previously reported to be useful prognostic indicators in CRC. For example, Lino-Silva *et al* (57) included 392 patients of all stages and found that stage I-III patients who presented with TDs displayed similar mortality rates to stage IV patients.

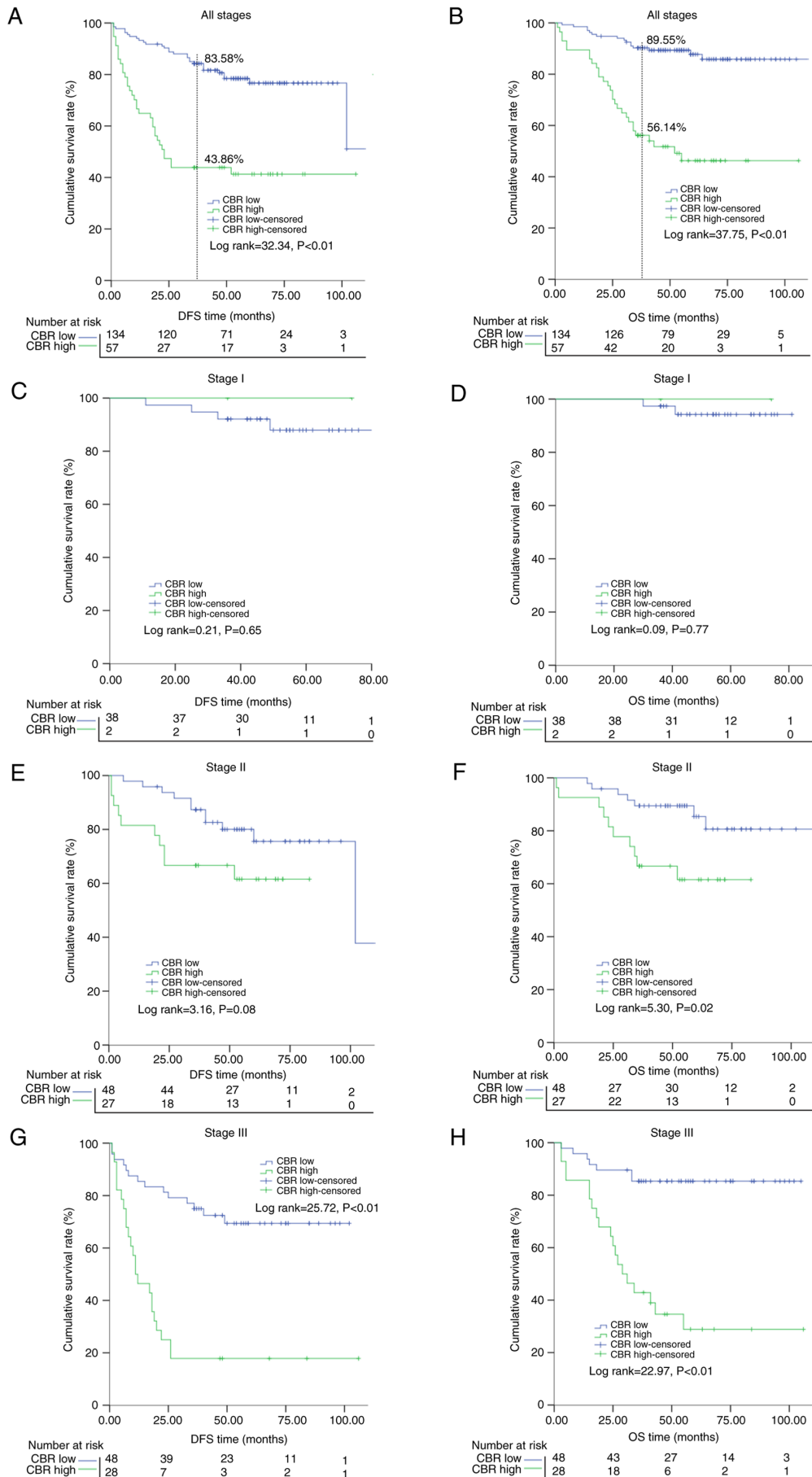


Figure 4. Differences between the high or low CBR subgroups for DFS in (A) all stages, (C) stage I and (E) stage II, and (G) stage III; and for OS in (B) all stages, (D) stage I and (F) stage II, and (H) stage III. The 3-year DFS and OS rates are indicated by the dotted lines in (A) and (B). CBR, carcinoembryonic antigen to body mass index ratio; DFS, disease-free survival; OS, overall survival.

Table II. Univariate and multivariate analyses of risk factors for disease-free survival.

Characteristic	Univariate			Multivariate		
	P-value	HR	95% CI	P-value	HR	95% CI
Age, years						
<60	1.00					
≥60	0.86	1.05	0.63-1.72			
Sex						
Female	1.00					
Male	0.27	1.36	0.79-2.35			
Type of resection						
Laparotomy	1.00					
Laparoscopy	<0.01 ^a	0.39	0.22-0.68			
Tumor location						
Right	1.00					
Left	0.84	0.94	0.52-1.71			
Histological grade						
Well + moderate	1.00					
Poor	0.08	1.74	0.94-3.22			
Mucinous element						
Present	1.00					
Absent	0.06	0.58	0.33-1.02			
T stages						
T ₁ + T ₂	1.00					
T ₃ + T ₄	<0.01 ^a	3.96	1.71-9.20			
N stages						
N ₀	1.00			1.00		
N ₁ + N ₂	<0.01 ^a	2.85	1.71-4.74	<0.01 ^a	2.30	1.30-4.08
Tumor deposits						
Present	1.00			1.00		
Absent	<0.01 ^a	0.13	0.07-0.24	<0.01 ^a	0.34	0.17-0.67
TNM stages						
I	1.00					
II	0.05 ^a	2.98	1.02-8.69			
III	<0.01 ^a	6.45	2.30-18.14			
Risk factors						
Present	1.00					
Absent	0.01 ^a	0.43	0.23-0.79			
Preoperative measures						
NLR	<0.01 ^a	1.08	1.03-1.14			
LMR	0.02 ^a	0.82	0.69-0.97			
PLR	0.02	1.00	1.00-1.01			
PNI	<0.01 ^a	0.93	0.90-0.97	<0.01 ^a	0.93	0.90-0.97
CBR						
Low	1.00			1.00		
High	<0.01 ^a	3.86	2.33-6.37	<0.01 ^a	3.48	2.04-5.91

^aP<0.05. TNM, Tumor-Node-Metastasis; CBR, carcinoembryonic antigen to body mass index ratio; NLR, neutrophil to lymphocyte ratio; LMR, lymphocyte to monocyte ratio; PLR, platelet to lymphocyte ratio; PNI, prognostic nutritional index.

Furthermore, Moon *et al* (58) published a systematic review that included 90,455 stage III patients and found that those

who presented with TDs had a worse 5-year DFS rate. In addition to TDs, the association of a low LMR with poor survival

Table III. Univariate and multivariate tests of risk factors for overall survival.

Characteristic	Univariate			Multivariate		
	P-value	HR	95% CI	P-value	HR	95% CI
Age, years						
<60	1.00					
≥60	0.13	1.60	0.88-2.93			
Sex						
Female	1.00					
Male	0.20	1.54	0.80-2.99			
Type of resection						
Laparotomy	1.00					
Laparoscopy	0.03 ^a	0.47	0.24-0.93			
Tumor location						
Right	1.00					
Left	0.96	0.98	0.47-1.98			
Histological grade						
Well + moderate	1.00			1.00		
Poor	0.01 ^a	2.32	1.20-4.50	0.01 ^a	2.54	1.26-5.11
Mucinous element						
Present	1.00			1.00		
Absent	0.04 ^a	0.50	0.26-0.95	0.05 ^a	0.49	0.24-0.98
T stages						
T ₁ + T ₂	1.00					
T ₃ + T ₄	0.01 ^a	4.12	1.48-11.51			
N stages						
N ₀	1.00					
N ₁ + N ₂	<0.01 ^a	2.38	1.32-4.30			
Tumor deposits						
Present	1.00			1.00		
Absent	<0.01 ^a	0.12	0.06-0.23	<0.01 ^a	0.24	0.12-0.47
TNM stages						
I	1.00					
II	0.03 ^a	4.87	1.12-21.07			
III	<0.01 ^a	8.23	1.95-34.70			
Risk factors						
Present	1.00			1.00		
Absent	<0.01 ^a	0.34	0.17-0.67	0.01 ^a	0.37	0.18-0.78
Preoperative measures						
NLR	0.01 ^a	1.09	1.03-1.16			
LMR	0.04 ^a	0.82	0.67-0.99			
PLR	0.04 ^a	1.00	1.00-1.01			
PNI	<0.01 ^a	0.91	0.87-0.95	<0.01 ^a	0.89	0.85-0.94
CBR						
Low	1.00			1.00		
High	<0.01 ^a	5.50	2.98-10.15	<0.01 ^a	3.71	1.95-7.08

^aP<0.05. TNM, Tumor-Node-Metastasis; CBR, carcinoembryonic antigen to body mass index ratio; NLR, neutrophil to lymphocyte ratio; LMR, lymphocyte to monocyte ratio; PLR, platelet to lymphocyte ratio; PNI, prognostic nutritional index.

was also recorded; for example, Naszai *et al* (59) conducted a meta-analysis that included 32,788 patients and found that a

pre-treatment high NLR was a significant predictor of poor OS. In line with this, Tan *et al* (4) also conducted a meta-analysis

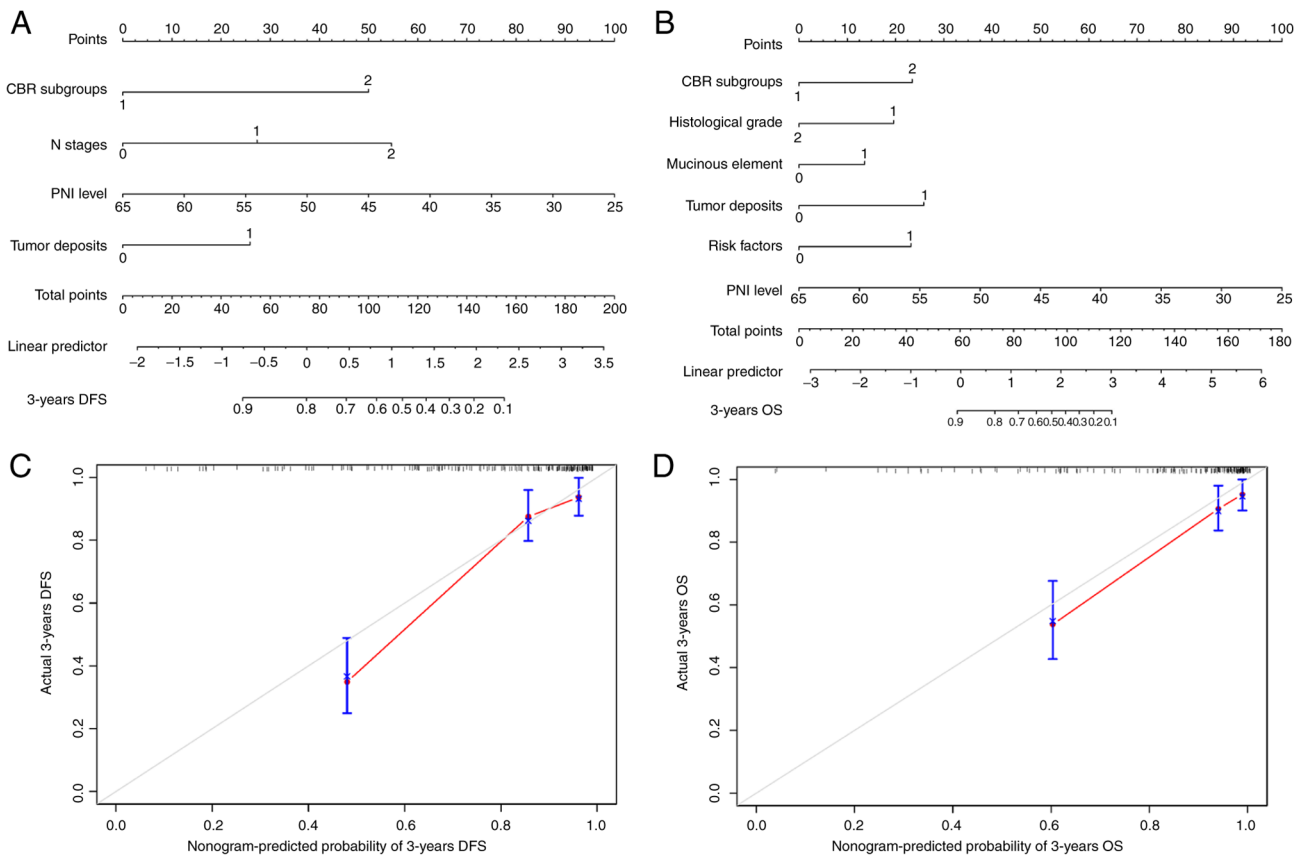


Figure 5. Nomograms for predicting the 3-year (A) DFS and (B) OS rates, and the calibration curves of the nomograms for predicting the 3-year (C) DFS and (D) OS rates. CBR, carcinoembryonic antigen to body mass index ratio; PNI, prognostic nutritional index; DFS, disease-free survival; OS, overall survival.

that concluded that a low LMR was a significant predictor of poor OS. All this evidence supports the fact that patients with CRC and a high CBR have poor survival rates.

In recent years, a small subgroup of patients with CRC featuring mismatch repair deficiency (dMMR) were demonstrated to exhibit better outcomes than those with mismatch repair-proficient tumors (pMMR) in certain stage cases, such as stage II (60,61), and they also had a significantly good response when receiving immunotherapies in metastatic cases when compared to pMMR cases (62). Notably, a lower BMI was found to be more common in patients with dMMR than in those with pMMR (63); additionally, CEA levels were significantly higher in the pMMR subtype (but only in stage III patients) (64). These results suggested that for patients in certain stages, the CBR would be higher than for those in other stages. However, in the present study, no such differences were found either for BMI (n=112, P=0.64; data not shown) or for CEA levels (n=47, P=0.92; data not shown). Taking into consideration the complex prognostic role of MMR status in CRC, additional studies with larger samples are still needed.

The present study also had some limitations. First, it was conducted with a relatively small sample size; in particular, the patients with a follow-up time of <36 months were excluded since these cases may lack definite OS information and cause problems in calculating the specific survival rate, which may also result in a biased finding. Second, both CEA levels and BMI could present extreme values, and the prognostic value of the CBR was not validated in these cases. Third, definite

information for those stage II patients with high risks or the stage III patients on adjuvant therapy was not sufficient, and it was well established that adjuvant chemotherapy could improve the DFS in patients with radical surgery (65,66). However, it was notable that a number of other factors could influence the efficacy of these therapies in the real world, including the delay, early discontinuation and dose reduction of the treatment. This is a complex problem that requires additional elegant studies. Further studies are also needed to further validate the present results.

Overall, the present results indicated that, compared with individual CEA, BMI, NLR and LMR values, the CBR was a more robust prognostic factor in CRC, and patients with a relatively high CBR presented with inferior survival rates.

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Availability of data and materials

The datasets used and/or analyzed during the current study are available from the corresponding author on reasonable request.

Authors' contributions

BY was responsible for the conception of the work. JX, MD and JL obtained the data and contributed to the data analysis. TX, QY and BY checked and analyzed the data. BY wrote the manuscript. JX and BY confirm the authenticity of all the raw data. All authors read and approved the final manuscript.

Ethics approval and consent to participate

The study was performed in line with the principles stated in the Declaration of Helsinki and was approved by the Ethics Committee of Hainan Hospital of Chinese People's Liberation Army General Hospital (approval no. 301HLFYLS15). The patients or their authorized relatives provided written informed consent.

Patient consent for publication

Not applicable.

Competing interests

The authors declare that they have no competing interests.

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