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Prognostic value of preoperative D-dimer to albumin ratio in patients with locally advanced rectal cancer after neoadjuvant chemoradiotherapy

Zhen Pan[1] · Ye Wang[1] · Shoufeng Li[1] · Huajun Cai[1] · Guoxian Guan[1,2]

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Abstract

Background The prognostic value of Albumin and D-dimer has been established for multiple tumor types, indicating their potential for predicting tumor development. Nevertheless, the predictive capability of the DDI-to-albumin ratio (DAR) in locally advanced rectal cancer (LARC) remains uncertain.

Purpose The objective of this study was to investigate the prognostic significance of the DAR in LARC.

Methods A total of 513 patients who underwent neoadjuvant chemoradiotherapy (nCRT) prior to total mesorectal excision (TME) between March 2013 to October 2019 were included in this study. Patients were divided into high-level DAR (> 0.016) or low-level DAR (≤ 0.016) groups based on ROC curve analysis optimum cut-off value. The prognostic value of the DAR in LARC was analyzed.

Results The study enrolled 513 patients. Patients were stratified into high-level DAR (> 0.016) and low-level DAR (≤ 0.016) cohorts according to the optimal cut-off value determined by ROC curve analysis. The 5-year overall survival (OS) rates for patients in the low DAR group (≤ 0.016) and the high DAR group (> 0.016) were 89.4% and 80.9%, respectively (p = 0.013). The 5-year disease-free survival (DFS) rates were 85.7% and 77.4% (p = 0.027). Multivariate analyses demonstrated that DAR were independent prognostic factors for OS (p = 0.02) and DFS (0.025). Predictive nomograms that included the DAR score group (C-index: OS-0.743, DFS-0.705) were superior to those without DAR scores (C-index: OS-0.721, DFS-0.697).

Conclusion The DAR demonstrates high usability and prognostic value in predicting OS and DFS outcomes among patients diagnosed with LARC who undergo nCRT.

Keywords DDI-to-albumin ratio · Locally advanced rectal cancer · Neoadjuvant chemoradiotherapy · Prognosis · Nomograms

1 Introduction

In recent years, the prevalence of locally advanced rectal cancer (LARC) continues to be substantial [1]. Currently, the standard treatment for LARC is neoadjuvant chemoradiotherapy (nCRT) and total mesorectal excision(TME) [2–4]. The utilization of nCRT has been found to effectively downstage LARC, resulting in a reduction in postoperative local recurrences [5, 6]. This

Zhen Pan, Ye Wang and Shoufeng Li have contributed equally to this work.

✉ Guoxian Guan, fjxhggx@163.com | [1]Department of Colorectal Surgery, The First Affiliated Hospital of Fujian Medical University, Fuzhou, China. [2]Department of Colorectal Surgery, National Regional Medical Center, Binhai Campus of the First Affiliated Hospital, Fuzhou, China.

approach significantly enhances the management of local tumors, improves resectability, and facilitates tumor shrinkage and downstaging [7–9]. Nevertheless, among patients with LARC, neoadjuvant therapy has a heterogeneous response, resulting in varying long-term outcomes. Patient prognoses determine adjuvant treatment and surveillance. There remains difficult to predict LARC patients' treatment outcomes after nCRT accurately. Therefore, the identification of dependable biomarkers for oncologic outcomes holds significant importance in aiding risk-adapted treatment strategies and subsequent surveillance.

Prior research has demonstrated a correlation between cancer patients and aberrant blood clotting functionality [10–12]. The activation of blood coagulation and procoagulant alterations at a systemic level were found to be linked with processes such as angiogenesis, invasion and progression of tumor cells, as well as the spread of metastases [13]. D-dimer, an end-degradation product of fibrin degradation, serves as an indicator of hemostasis activation and the presence of a hypercoagulable state. Increased levels of D-dimer have been observed in various conditions such as acute venous thromboembolism, pregnancy, infectious diseases, surgical procedures, and malignancies [14]. Moreover, recent studies showed that elevated D-dimer levels predicted poor prognosis in various types of cancer, including colorectal cancer [13]. Albumin, a commonly employed nutritional marker, has been recognized as a prospective indicator of inflammation. Multiple studies have demonstrated a correlation between Albumin and cancer, with Albumin serving as a prognostic indicator for predicting the outcomes of malignancies, including colorectal cancer [16, 17].

Hence, in accordance with prior research, it has been established that D-dimer and albumin possess the ability to individually forecast the prognosis of individuals diagnosed with LARC. The combination of D-dimer and Alb, defined as DAR, has been shown to be associated with the prognosis of multiple tumors [18, 19]. Furthermore, when compared to the individual biomarkers of albumin and D-dimer, the combined assessment of DDI and albumin demonstrates enhanced predictive capabilities in identifying hypercoagulability and malnutrition among cancer patients, thereby increasing the accuracy of prognostic evaluations. According to Lin et al., the DDI-to-albumin ratio (DAR) could be used to predict long-term survival for GC patients [18]. In another study by He et al., combining D-dimer with albumin was also found to predict DFS and OS in nasopharyngeal carcinoma patients [19]. However, the prognostic significance of the DAR in patients with LARC who have undergone nCRT remains uncertain.

In this study, we combined albumin and D-dimer and developed and defned the D-dimer to albumin ratio (DAR) to explore the prognostic association between DAR and LARC.

1.1 Methods

1.1.1 Patients and study design

A total of 513 LARC patients who received nCRT between March 2013 and October 2019 were included. Inclusion criteria: (1) Rectal cancer with pathological confirmation; (2) Blood routine and biochemical examination were improved before surgery; (3) Ages 18–80. Exclusion criteria: (1) Rectal polyp or adenoma; (2) Complicated with acute or chronic inflammatory diseases (like acute upper respiratory tract infection, pneumonia, acute pancreatitis, acute appendicitis, and pyelonephritis); (3) With other malignant tumors; (4) Incomplete clinical pathological information; (5) Stage IV rectal cancer; (6) Had history of thrombotic disease, receive anticoagulant therapy or antiplatelet therapy; (7) Acute infection or disseminated intravascular coagulation. Physical examination, anoscopy, chest CT, abdominal-pelvic CT, endorectal ultrasound, transrectal ultrasound, and magnetic resonance imaging indicated tumor staging. Surgical procedures were performed 6- to 8-weeks after radiation treatments were completed. NCCN [20] guidelines recommend postoperative adjuvant chemotherapy one month following surgery. Based on NCCN [20] guidelines, a follow-up program was implemented. The Ethics Committee of Fujian Medical University's First Affiliated Hospital approved this study.

1.2 Treatment strategy

All patients were administered preoperative radiation therapy at a dose of 45 Gy/25, delivered to the pelvic over a period of 5 weeks. This was followed by a boost of 5.4-Gy specifically targeting the primary tumor. The preoperative concurrent chemoradiotherapy regimens employed were CapeOX (capecitabine plus oxaliplatin), Capecitabine and FOLFOX (5FU plus oxaliplatin). The surgical intervention is typically conducted within a timeframe of 6 to 8 weeks following the

conclusion of radiation therapy. Middle and low rectal cancers were managed through TME, while high rectal cancers were addressed through partial TME, ensuring a distal margin of 5 cm. Subsequently, patients received postoperative adjuvant chemotherapy approximately 4–8 weeks after the surgical procedure, irrespective of the outcomes of the surgical pathology assessment.

1.3 Definitions

Pathological complete response (pCR) is the absence of tumor cells in the primary site and resected lymph nodes. A routine blood test was conducted at the time of the first cancer diagnosis. Locally advanced rectal cancer (LARC) is defined as rectal cancer located within 12 cm from the anal verge, without evidence of distant metastases (M0), is present in the mesorectal and true pelvic regions. The disease is characterized by lymph node involvement (c/pN1-2) and invasion of the muscularis propria by the primary tumor, as confirmed through imaging or pathological assessment. DAR is defined as the preoperative ratio of DDI to albumin. This study calculated overall survival (OS) from the surgical date to the last follow-up or death date (specifically, cancer-related deaths were not considered). Disease-free survival (DFS) was the survival time until a local or distant disease recurred.

1.4 Statistical analysis

Statistical analyses were conducted using the SPSS 22.0 software package and the R statistical package (http://cran.r-project.org/). The chi-square test or Fisher's exact test was employed for the analysis of categorical variables, while the analysis of continuous variables involved the use of Student's t-test or the Mann–Whitney U test. An analysis of overall survival results (survival rates) was performed using the Kaplan–Meier (KM) method. A Cox regression model was utilized to determine risk factors for OS and DFS. Then, a nomogram was constructed based on the final predictive model by using R statistical package with the survival and rms package. The nomogram was validated internally (1000 bootstrap resamples) to correct for overfitting. A bootstrapping method is a nonparametric data generating method in which new datasets are repeatedly generated from an original dataset and created by random drawing from the sample with replacement. The predictive performance of the nomogram was assessed by calculating Harrell's concordance index (c-index). Nomogram calibration for 3- and 5-year OS and DFS was performed by comparing the predicted and actual probability after bias correction. It is defined as statistically significant when $P < 0.05$.

2 Results

2.1 Patient characteristics

A total of 513 patients with LARC who underwent nCRT were included in the database, of whom 329 were men and 184 were women, for all patients, the median follow-up time was 77.3 months. On the basis of the ROC analysis, the cutoff value of the DAR was 0.016. Based on the above cut of points, we divided the entire cohort into low-DAR($DAR \leq 0.016$) and high-DAR($DAR > 0.016$) groups. Table 1 provides a comprehensive overview of the clinical characteristics exhibited by both groups. The analysis reveals that there is no statistically significant distinction observed between the two groups.

2.2 Association of DAR with survival

ROC curve analysis using the R package ROCR determined the optimal DAR cut-off point. To categorize our cohort according to the above cut-off points, we divided them into low and high subgroups in OS and DFS. High-DAR LARC patients had a worse prognosis after nCRT. In the low DAR groups, OS rates at five years were 89.4%, significantly higher than 80.9% in the high DAR groups ($P = 0.013$, Fig. 1A). Notably, a significant association exists between lower DAR scores and better DFS. DFS rates at five years for the low DAR group are 85.7%, compared to 77.4% for the high DAR group ($P = 0.027$, Fig. 1B).

Table 1 Clinicopathologic characteristics of all the patients

Characteristics	DAR ≤ 0.016(n = 396)	DAR > 0.016(n = 117)	P-value
Age (year), mean (SD)	55.67 ± 10.61	57.74 ± 11.76	0.072
Interval time between NCRT and surgery (day), mean (SD)	66.94 ± 23.98	66.03 ± 10.20	0.690
Distance from the anal verge (cm), mean (SD)	6.69 ± 2.37	6.60 ± 2.79	0.732
Tumor size(cm), mean (SD)	2.59 ± 1.19	2.57 ± 1.36	0.854
Postoperative hospital stay(day), mean (SD)	8.34 ± 5.32	8.54 ± 5.20	0.730
Total hospitalization day(day), mean (SD)	19.88 ± 6.93	20.55 ± 6.66	0.359
Sex (%)			0.078
Female	134(72.8)	50(27.2)	
Male	262(79.6)	67(20.4)	
ASA score, n(%)			0.141
I	276(79.8)	70(20.2)	
II	115(71.9)	45(28.1)	
III	5(71.4)	2(28.6)	
ypTNM stage (8th AJCC), n(%)			0.890
pCR	93(76.2)	29(23.8)	
I	99(76.2)	31(23.8)	
II	109(76.8)	33(23.2)	
III	95(79.8)	24(20.2)	
APR, n(%)			0.522
No	36,677.5)	106(22.5)	
Yes	30(73.2)	11(26.8)	
Neural invasion			0.884
No	377(77.3)	111(22.7)	
Yes	19(76.0)	6(24.0)	
Lymphovascular invasion			0.694
No	383(77.1)	114(22.9)	
Yes	13(81.3)	3(18.8)	
Radiotherapy complication			0.305
No	264(78.6)	72(21.4)	
Yes	132(74.6)	45(25.4)	
Postoperative complication			0.964
No	331(77.2)	98(22.8)	
Yes	65(77.4)	19(22.6)	
Adjuvant chemotherapy			0.152
No	102(72.9)	38(27.1)	
Yes	294(78.8)	79(21.2)	
TRG grade, n(%)			0.434
0	95(77.2)	28(22.8)	
1	129(76.8)	39(23.2)	
2	153(79.3)	40(20.7)	
3	19(65.5)	10(34.5)	
Chemotherapy, n(%)			0.099
CapeOX	42(66.7)	21(33.3)	
Capecitabine	321(78.9)	86(21.1)	
FOLFOX	33(76.7)	10(23.3)	

DAR: DDI-to-albumin ratio; LARC: locally advanced rectal cancer; NCRT: neoadjuvant chemoradiotherapy; ASA: American Society of Anesthesiologists; TRG grade: tumor regression grade. APR: abdominoperineal resection

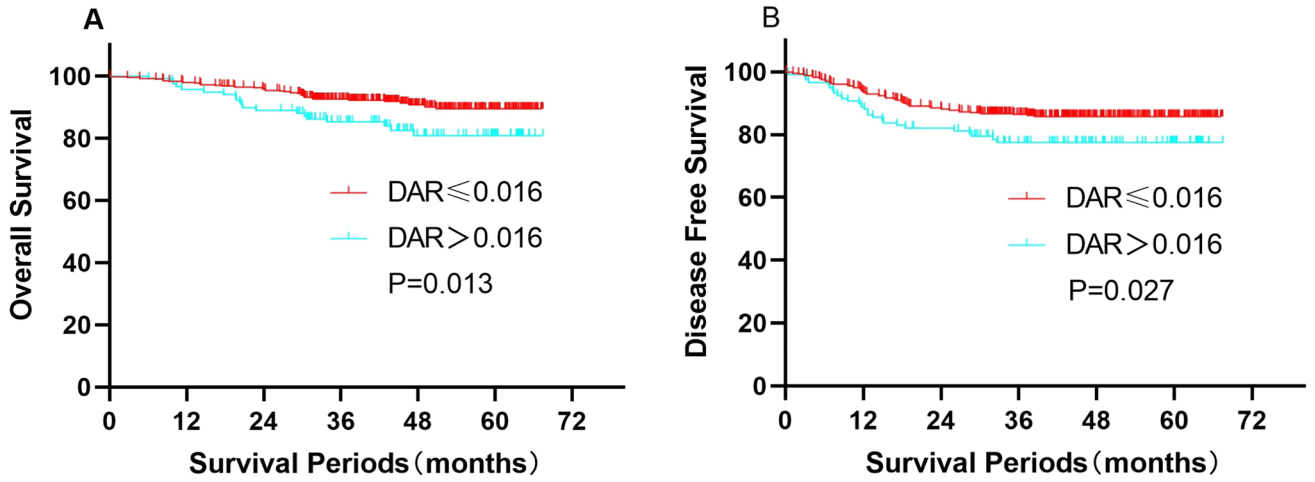

Fig. 1 Kaplan–Meier analysis of the DAR counts. The overall survival **A** and disease-free survival **B** for the optimal cutoff point of the DAR counts. The entire cohort was divided into low (blue) and high (red) DAR count groups based on the optimal cutoff point (0.016)

2.3 Association of DAR with prognostic

In order to investigate the prognostic significance of DAR on OS and DFS in patients with LARC, a COX regression analysis was conducted. In the univariate analysis, several factors including the tumor size ($P < 0.001$), pathological TNM stage ($P < 0.001$), TRG grade ($P < 0.001$), neural invasion ($P = 0.001$), and DAR level ($P = 0.015$) were found to be independently associated with OS in patients with LARC who underwent nCRT and TME(Table 2). The Cox regression analysis revealed that the pathological TNM stage ($P = 0.047$), the tumor size (HR = 1.231, 95%CI: 1.023–1.481, $P = 0.028$), and the DAR level (HR = 1.941, 95%CI: 1.112–3.387, $P = 0.002$) were identified as significant independent predictors of OS following nCRT, as presented in Table 2.

In the analysis conducted, several factors were found to be independently associated with DFS in patients with LARC who underwent nCRT and TME. These factors included the tumor size ($P < 0.001$), pathological TNM stage ($P < 0.001$), TRG grade ($P = 0.002$), distance from the anal verge ($P = 0.046$), the DAR level ($P = 0.025$), and neural invasion ($P = 0.015$), as shown in Table 3. The results of the Cox regression analysis revealed that the pathological TNM stage ($P = 0.007$), the long diameters of tumor (HR = 0.898, 95%CI: 0.817–0.986, $P = 0.024$), the DAR level (HR = 1.715, 95%CI: 1.069–2.751, $P = 0.025$), and distance from the anal verge (HR = 0.898, 95%CI: 0.817–0.986, $P = 0.024$) were identified as independent predictors of DFS after nCRT according to Table 3.

2.4 OS and DFS prediction models with/without DAR

Predictive nomograms for OS and DFS in patients with LARC following nCRT were developed based on the aforementioned significant determinants (Fig. 2A, B). The predictive probabilities for 3-year OS and disease-free survival DFS were determined by summing the scores of each variable and plotting a linear regression line. Patients with higher total scores exhibited a tendency towards lower rates of OS and DFS. The internal validation of the model demonstrated its performance. The C-index of the nomogram, which incorporated DAR as a predictor for OS and DFS, was calculated as 0.743 (95%CI: 0.714–0.772) and 0.705 (95%CI: 0.677–0.733), respectively. To further explore the role of the DAR in the predictive model, we constructed another model without DAR (Fig. 3A, B). The C-index of the nomogram without DAR for predicting OS and DFS was 0.721 (95%CI: 0.691–0.751) and 0.697 (95%CI: 0.670–0.724), respectively.The calibration curves showed good agreement between the predicted and actual probability of 3-, and 5-year OS (Fig. 4A, C) and DFS (Fig. 4B, D).

2.5 Validation of the model

Furthermore, a Decision Curve Analysis (DCA) was performed, employing the net benefit rate as an ordinal measure, while setting the high-risk threshold to a negative value of (0.1) (Fig. 5). As depicted in Fig. 5, the net benefit rate exceeded 0 within the high-risk threshold range of 0–1, indicating clinical significance.

Table 2 Univariate and multivariable analysis of overall survival

Variable	Univariate analysis		Multivariate analysis	
	HR (95%CI) P-value		HR (95%CI) P-value	
Mean, age (year)	0.993(0.969–1.017)	0.542		
Mean, distance from the anal verge(cm)	0.987(0.885–1.102)	0.821		
Mean, interval time between NCRT and surgery (day)	0.996(0.978–1.014)	0.655		
Mean, postoperative hospital stay(day)	1.009(0.963–1.056)	0.712		
Mean, tumor size(cm)	1.456(1.230–1.722)	**< 0.001**	1.231(1.023–1.481)	**0.028**
Mean, total hospitalization day(day)	1.028(0.998–1.058)	0.065		
Sex		0.638		
Female	1			
Male	1.145(0.652–2.011)			
ASA score, n(%)		0.589		
I	1			
II	1.308(0.756–2.263)	0.336		
III	1.604(0.219–11.730)	0.642		
ypTNM stage (8th AJCC), n(%)		**< 0.001**		
pCR	1		1	**0.047**
I	2.225(0.575–8.606)	0.246	1.567(0.064–38.222)	0.783
II	5.921(1.752–20.012)	**0.004**	3.487(0.153–79.523)	0.434
III	10.049(3.041–33.208)	**< 0.001**	5.112(0.235–111.084)	0.299
DAR level		**0.015**		**0.020**
≤ 0.016	1		1	
> 0.016	1.977(1.141–3.426)		1.941(1.112–3.387)	
Adjuvant chemotherapy		0.067		
No	1			
Yes	0.601(0.349–1.036)			
Postoperative complication		0.496		
No	1			
Yes	0.759(0.343–1.678)			
Radiotherapy complication		0.906		
No	1			
Yes	0.967(0.556–1.683)			
Neural invasion		**0.001**		0.446
No	1		1	
Yes	3.681(1.656–8.182)		1.404(0.587–3.359)	
Lymphovascular invasion		0.721		
No	1			
Yes	1.294(0.315–5.309)			
APR, n(%)		0.683		
No	1			
Yes	1.211(0.483–3.038)			
TRG grade(%)		**< 0.001**		0.281
0	1		1	
1	4.316(1.265–14.729)	**0.020**	1.340(0.059–30.582)	0.854
2	5.689(1.717–18.842)	**0.001**	1.489(0065–33.917)	0.803
3	18.174(5.000–66.061)	**< 0.001**	3.000(0.128–70.117)	0.494
Chemotherapy, n(%)		0.515		
CapeOX	1			
Capecitabine	1.742(0.627–4.846)	0.287		
FOLFOX	2.015(0.568–7.147)	0.278		

Bold indicates that the *P* value is less than 0.05, which is significant

DAR: DDI-to-albumin ratio; LARC: locally advanced rectal cancer; NCRT: neoadjuvant chemoradiotherapy; ASA: American Society of Anesthesiologists; TRG grade: tumor regression grade. APR: abdominoperineal resection

3 Discussion

Previous studies have established a robust association between DAR and the progression and prognosis of cancer. However, the specific impact of DAR on LARC patients undergoing nCRT remains uncertain. The objective of this study was to assess the predictive value of DAR in determining the prognosis of LARC patients undergoing nCRT. To the best of our knowledge, this is the first investigation to utilize DAR as a prognostic indicator for LARC. The findings of this study indicate that the DAR variable operates as an independent prognostic factor for LARC patients following nCRT. Furthermore, a prognostic nomogram was developed by incorporating DAR, and its performance was assessed through DCA and calibration curve analysis.

Hypercoagulability is closely associated with malignancy [19, 20]. Cancer cells' cytokines and proteins disrupt normal cell activities, disturb the balance between fibrolysis and anticoagulation, damage vascular endothelial cells, release cytokines and coagulants, encourage tumor cell migration and invasion, and tumor vascular leakage [23]. Consequently, anticoagulants are vital in tumor treatment [22]. The D-dimer is a clinically useful product of coagulation, a product of fibrinolysis, and is found in the blood after fibrinolysis breaks down blood clots. The D-dimer is important in many human cancers [25]. First reported in 1993, Edwards et al. [26] found colorectal cancer is correlated with D-dimer, and subsequent studies supported this finding. D-dimer has been shown to be a prognostic marker after primary colorectal cancer lesions resection [27–29] and an indicator of the therapeutic effect of chemotherapy in colorectal cancer [30]. Oya et al. [31] found that preoperative D-dimer elevation in colorectal cancer patients is linked with pathological T factor, tumor size, and shorter overall survival. Despite these D-dimer investigations, there are no reports on the prognosis of locally progressed rectal cancer after neoadjuvant chemoradiotherapy.

Aside from hypercoagulability, the relationship between poor nutritional status and tumors also deserves attention. Hypoalbuminemia can decrease immune response and make antitumor treatment less effective. Serum albumin is used to measure nutritional status [32]. Moreover, systemic inflammatory conditions are associated with serum albumin levels. For example, inflammatory factors like IL-6 and IL-4 inhibit hepatocytes from making albumin and reduce serum levels [33]. Thus, preoperative serum albumin levels can indicate cancer prognosis, inflammation, and nutrition. However, combined with other system inflammatory indicators, albumin predicts cancer prognosis more accurately than albumin alone. For instance, the GPS (Glasgow prognostic score), introduced by Forrest et al., is a well-known inflammation-related marker that includes serum C-reactive protein (CRP) levels and serum albumin levels, predicting the CRC prognosis [34]. Another study by Liu et al. found that serum albumin and preoperative plasma D-dimer levels significantly impacted the postoperative survival of patients having transthoracic esophagectomy for esophageal squamous cell cancer [35].

The DAR score, which combines the nutritional index Alb and the hypercoagulability index DDI, has recently emerged as a convenient and effective tool. Zhang et al [36]. Demonstrated that the ratio of albumin to DDI has the potential to serve as a valuable indicator for prognostic assessment and evaluation of chemotherapy effectiveness in patients with advanced gastric cancer who undergo neoadjuvant chemotherapy. Furthermore, the study revealed that the utilization of the albumin to D-dimer ratio as a prognostic indicator for chemotherapy efficacy and survival outperformed the individual assessment of albumin and D-dimer. Moreover, it was observed that patients with a diminished albumin to D-dimer ratio (< 41.64) exhibited a reduced disease control rate (77.9% vs. 92.5%, $P < 0.01$), shorter overall survival (271 vs. 389 days), and shorter progression-free survival (118 vs. 192 days) in comparison to patients with an elevated albumin to D-dimer ratio (≥ 41.64). In another investigation conducted by Lin GS [18] demonstrated that the preoperative DAR, based on plasma DDI and albumin, is a promising predictive biomarker for long-term prognosis in GC patients.

In the current investigation, the integration of DDI and albumin was employed to establish DAR, thereby concomitantly depicting hypercoagulability and malnutrition in LARC. Higher DAR scores (> 0.016) correlated with a poorer DFS and OS, which may be related to a hypercoagulable state, increased systemic inflammatory responses due to tumor consumption, or both. DAR is a dynamic characteristic that changes with treatment as a surrogate for tumor load. Therefore, DAR can better predict LARC's long-term prognosis. Using two predictive models with and without DAR, we further investigated DAR's prognostic significance in LARC patients. DAR-containing models predicted LARC patient DFS and OS better than models without DAR. The results of our study further confirmed that DAR plays a key role in predicting treatment outcomes in LARC patients after nCRT. In conclusion, a nomogram model was created to predict LARC prognosis, and DAR was crucial to this model. The findings of our study indicate that DAR serves as a

Table 3 Univariate and multivariable analysis of disease-free survival

Variable	Univariate analysis		Multivariate analysis	
	HR (95%CI) P-value		HR (95%CI) P-value	
Mean, age (year)	0.985(0.966–1.004)	0.132		
Mean, distance from the anal verge(cm)	0.908(0.826–0.998)	**0.046**	0.898(0.817–0.986)	**0.024**
Mean, interval time between NCRT and surgery (day)	0.996(0.982–1.011)	0.610		
Mean, postoperative hospital stay(day)	1.013(0.978–1.049)	0.470		
Mean, tumor size(cm)	1.338(1.155–1.550)	**< 0.001**	1.206(1.022–1.422)	**0.026**
Mean, total hospitalization day(day)	1.020(0.995–1.047)	0.120		
Sex		0.617		
Female	1			
Male	0892(0.570–1.396)			
ASA score, n(%)		0.919		
I	1			
II	0.905(0.561–1.460)	0.682		
III	0.928(0.128–6.704)	0.941		
ypTNM stage (8th AJCC), n(%)		**< 0.001**		
pCR	1		1	**0.007**
I	1.439(0.588–3.521)	0.425	3.187(0.412–24.669)	0.267
II	3.171(1.441–6.981)	**0.004**	6.303(0.870–45.680)	0.068
III	5.045(2.335–10.901)	**< 0.001**	8.315(1.222–56.596)	**0.030**
DAR level		**0.029**		**0.025**
≤ 0.016	1		1	
> 0.016	1.682(1.055–2.682)		1.715(1.069–2.751)	
Adjuvant chemotherapy		0.246		
No	1			
Yes	0.759(0.476–1.209)			
Postoperative complication		0.509		
No	1			
Yes	0.807(0.428–1.525)			
Radiotherapy complication		0.986		
No	1			
Yes	0.996(0.630–1.574)			
Neural invasion		**0.015**		0.751
No	1		1	
Yes	2.480(1.194–5.149)		1.139(0.509–2.552)	
Lymphovascular invasion		0.369		
No	1			
Yes	0.405(0.056–2.913)			
APR, n(%)		0.113		
No	1			
Yes	1.708(0.881–3.311)			
TRG grade(%)		**0.002**		0.480
0	1		1	
1	1.943(0.899–4.200)	**0.091**	0.398(0.060–2.639)	0.340
2	3.143(1.527–6.467)	**0.002**	0.547(0.084–3.556)	0.527
3	4.933(1.903–12.791)	**0.001**	0.654(0.089–4.791)	0.676
Chemotherapy, n(%)		0.207		
CapeOX	1			
Capecitabine	2.212(0.893–5.481)	0.086		
FOLFOX	1.733(0.529–5.678)	0.364		

Bold indicates that the *P* value is less than 0.05, which is significant

DAR: DDI-to-albumin ratio; LARC: locally advanced rectal cancer; NCRT: neoadjuvant chemoradiotherapy; ASA: American Society of Anesthesiologists; TRG grade: tumor regression grade. APR: abdominoperineal resection

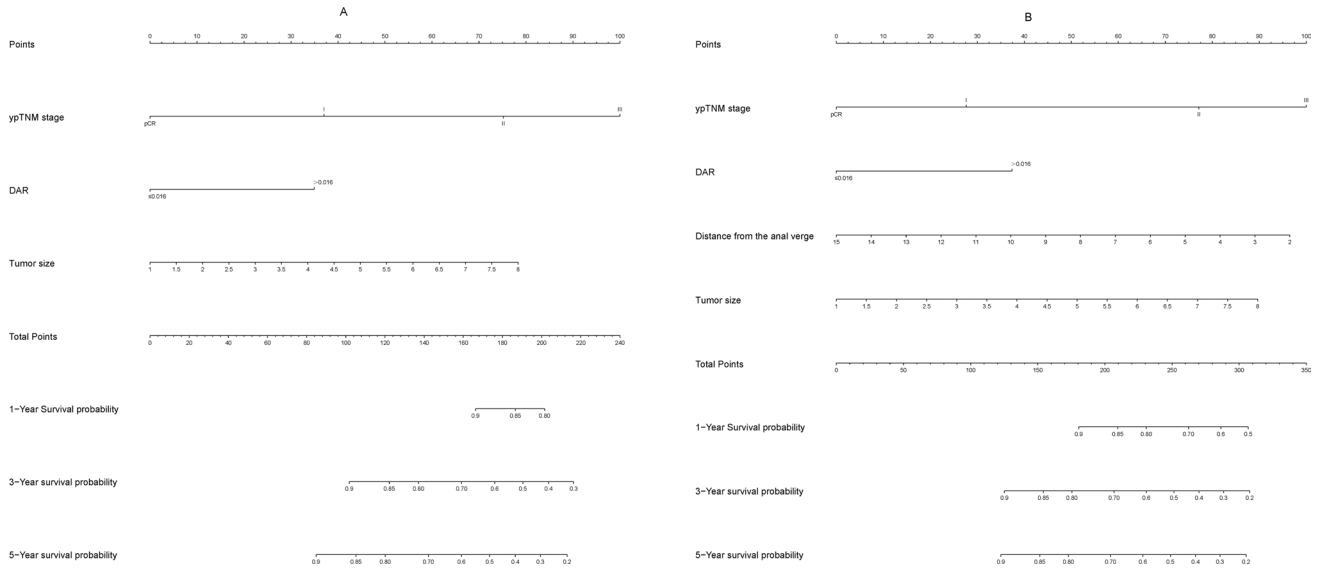

Fig. 2 Construction of the factors for overall survival/disease-free survival. **A** Nomograms with DAR developed for predicting overall survival. **B** Nomograms with DAR developed for predicting disease-free survival

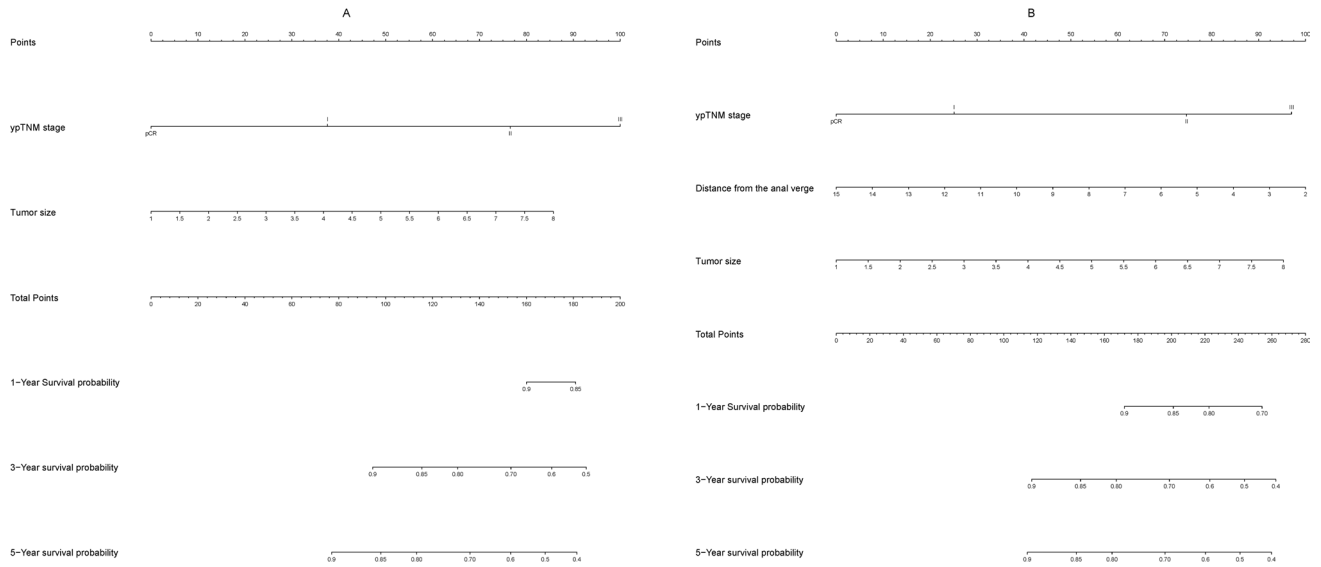

Fig. 3 Construction of the factors for overall survival/disease-free survival. (**A**) Nomograms without DAR developed for predicting overall survival. **B** Nomograms without DAR developed for predicting disease-free survival

cost-effective and readily available prognostic indicator, as well as a tool for predicting the benefits of chemotherapy. Furthermore, we recommend that DAR be regularly evaluated post-surgery and during the follow-up period.

Some limitations were present in our study. Since this was a retrospective single-center investigation, we require a prospective study design to evaluate our findings. Second, our sample size was limited. Thus, multicenter studies could provide a larger sample size for further investigation.

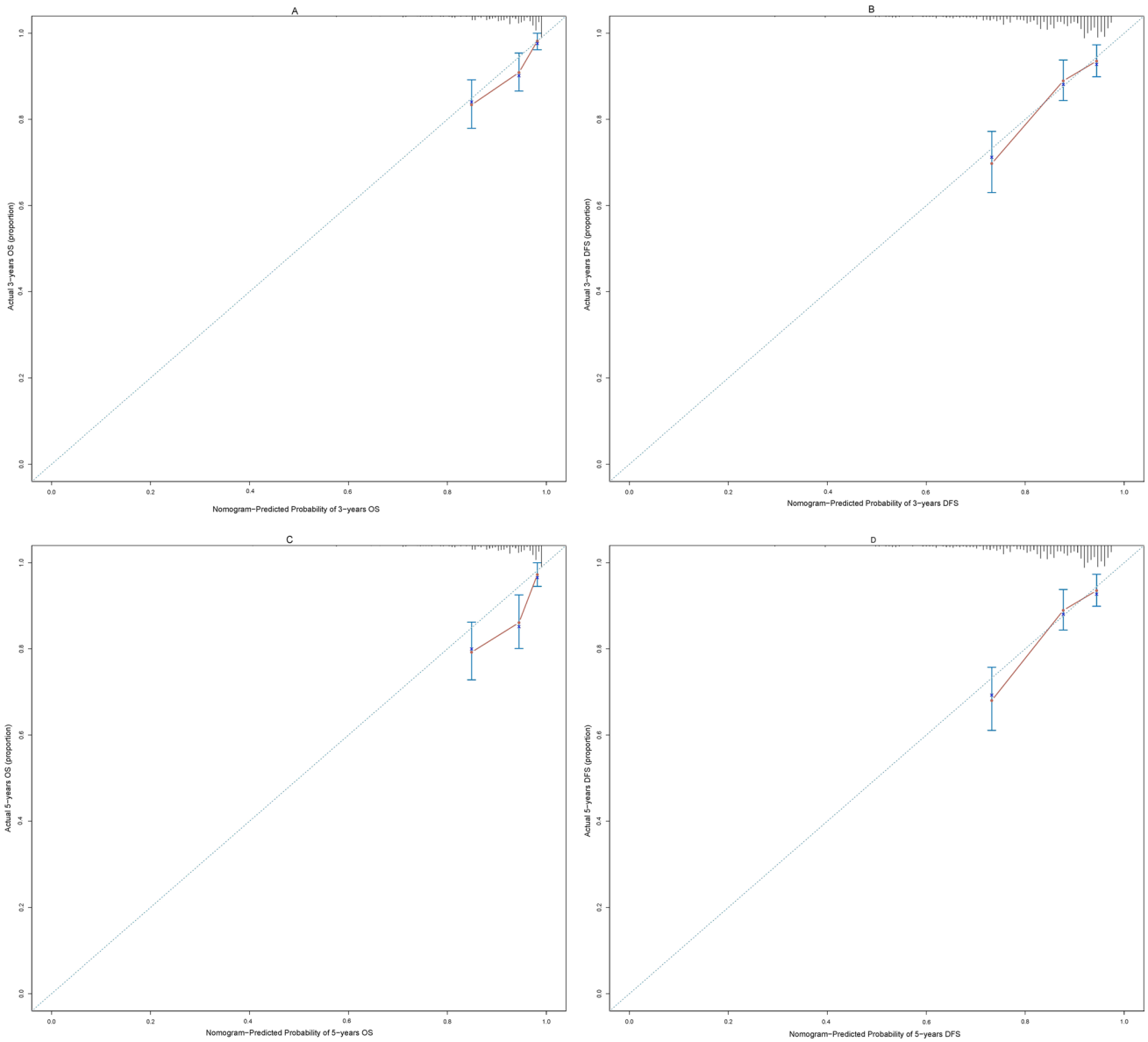

Fig. 4 **A** and **C** Calibration curves for 3- and 5-year OS for the model with DAR counts in LARC patients after nCRT with internal validation. **B**, **D** Calibration curves for 3- and 5-year DFS for the model with DAR counts in LARC patients after nCRT with internal validation

4 Conclusions

The DAR exhibits a notable level of usability and prognostic significance when used to forecast OS and DFS outcomes in patients diagnosed with LARC who undergo nCRT.

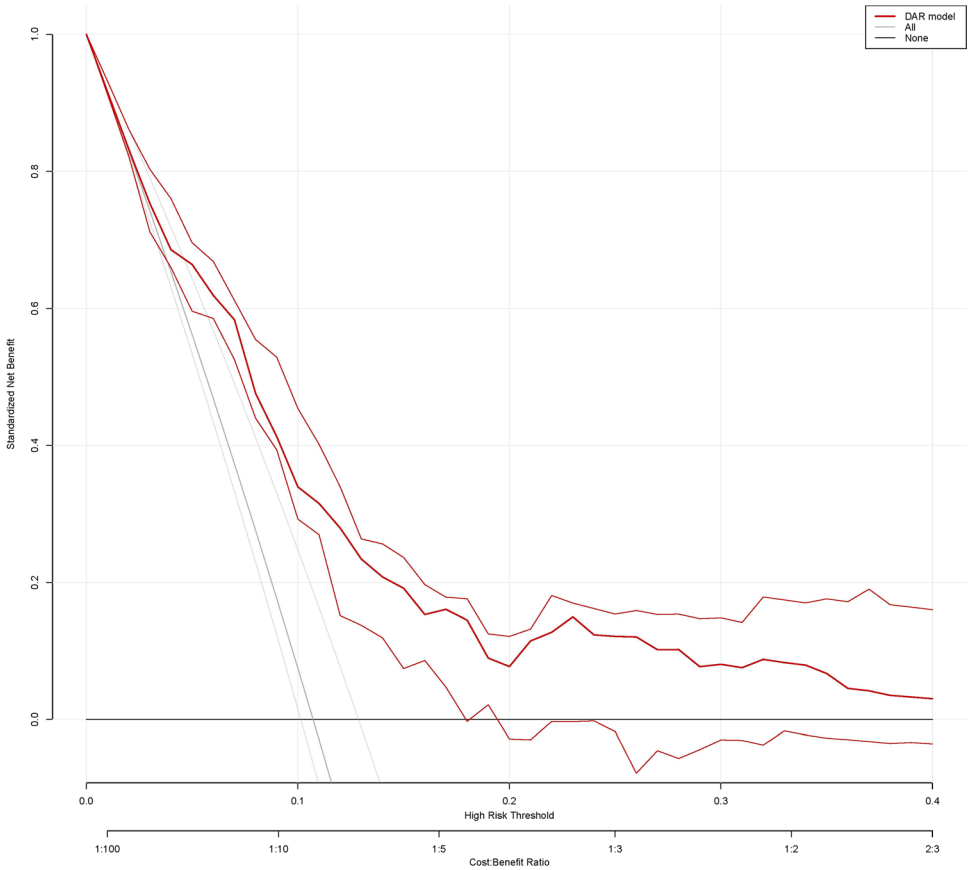

Fig. 5 Decision curve analysis curve of model △Alb-dNLR

Author contributions Conception and design were the responsibility of Zhen Pan, Acquisition of data was carried out by Shoufeng Li, and analysis were performed by Ye Wang and Huajun Cai. Interpretation, drafting, and revision of the manuscript were done by Guoxian Guan. All authors approved the final version of the manuscript.

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Data availability Some or all data used during the study are available from the corresponding author by request.

Declarations

Ethics approval and consent to participate This study was approved by Ethics Committee of The First Affiliated Hospital of Fujian Medical University and the approval number is 2021323. We confirm that the study was conducted in accordance with the relevant guidelines/regulations, and all participants and/or their legal guardians provided informed consent.

Consent for publication Informed consent for research purpose with patient data and images were obtained for all patients.

Competing interests All of the authors declare that they have no potential commercial conflicts of interest relevant to this article.

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