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World Journal of Surgical Oncology (2025) 23:160
https://doi.org/10.1186/s12957-025-03813-2

World Journal of Surgical Oncology

RESEARCH

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Prognostic impact of albumin-bilirubin score in predicting the long-term survival of distal cholangiocarcinoma after radical surgery

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Abstract

Background The Albumin-Bilirubin Score (ALBI) serves as an indicator of nutritional status and is a widely recognized prognostic biomarker in cancer patients. The purpose of this research is to evaluate the association between ALBI and survival outcomes in patients with distal cholangiocarcinoma (dCCA) after radical surgery, and develop a nomogram model based on the ALBI to predict individual survival.

Methods A total of 177 individuals with dCCA receiving surgery from Jan 2011 to Jan 2022 were enrolled in the research. The association between ALBI and clinicopathologic factors was investigated. The impact of ALBI on recurrence-free survival (RFS) and overall survival (OS) was evaluated by Kaplan–Meier curves and Cox proportional hazards models. Nomograms based on ALBI and other prognostic variables screened by multivariate analysis were produced in predicting RFS and OS of dCCA patients following radical surgery, and the nomograms were evaluated by the consistency index (C-index), calibration curve and decision curve analysis (DCA) curve.

Results The optimal cut-off value for ALBI was -1.67, and the area under the ROC curve (AUC) was 0.71. The High-ALBI group had a considerably shorter RFS and OS ($P < 0.001$). Multivariate analysis revealed that the ALBI, degree of differentiation, portal vein invasion, and lymph node invasion were significant prognostic factors for RFS, and that the ALBI, CA19-9, degree of differentiation, lymph node invasion, and portal vein invasion were significant prognostic factors for OS. The nomograms were constructed based on these significant prognostic factors. The calibration curves displayed good consistency between actual and predicted probability. Nomograms based on these variables have better discriminant ability in predicting RFS and OS compared with the American Joint Committee on Cancer (AJCC) TNM stage. Moreover, the scores predicted by the nomogram enabled patient stratification into low-points and high-points groups. Kaplan–Meier curves demonstrated that patients in the high-points group had considerably better prognoses than those in the low-points group ($p < 0.001$).

Conclusion ALBI was an independent prognostic factor in predicting RFS and OS of dCCA patients after radical surgery. The nomograms based on ALBI can provide reliable, personalized survival prediction for dCCA.

Keywords Distal cholangiocarcinoma, Albumin-bilirubin score, Nomogram, Prognosis

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Introduction

Distal cholangiocarcinoma (dCCA) is a malignancy originating from the distal segment of the common bile duct to the ampulla of Vater, constituting 20%− 40% of all cholangiocarcinoma [1, 2]. Notably, the incidence of dCCA is markedly higher in Asian countries as compared with Western nations [3]. Pancreatoduodenectomy (PD) is the most effective and standardized method in dealing with dCCA compared with other surgical procedures. Patients suffering from dCCA following radical surgery may achieve 5-year survival rates ranging from 13 to 54% [4], whereas those who do not have surgical resection experience a considerably lower 5-year survival rate of merely 3% [5]. Although comprehensive treatment regimens have shown significant effects in improving overall prognosis [6–8], radical surgical resection remains the primary treatment option for patients with dCCA. Consequently, precise prognostic assessment of dCCA patients following radical surgery plays a pivotal role in shaping more refined and effective treatment protocols.

The preoperative nutritional state has a considerable impact on the prognosis of cancer patients [9, 10]. Although ALBI, a novel nutritional evaluation score, has demonstrated its prognostic impact in several types of tumors [11, 12], its relationship with the survival outcomes of dCCA remains unexplored. Albumin is the main protein synthesized by the liver, reflecting its synthetic function, while total bilirubin is a metabolic waste product of the liver, with elevated levels typically indicating liver dysfunction. These two factors are combined in the ALBI score, which provides a comprehensive assessment of liver function and can predict clinical outcomes of patients. Therefore, we believe that a higher ALBI score may reflect poorer liver function, which may affect the long-term prognosis of patients with dCCA. Physicians may apply nomograms, predictive models capable of integrating several prognostic signals, to boost the accuracy of forecasting patient survival [13–15]. Despite the widespread use of nomograms in various prognostic assessments, few have been developed for predicting the survival outcomes of dCCA patients.

Therefore, this study proposes to explore the impact of ALBI on the survival outcomes of dCCA patients following radical surgery, and to create an innovative nomogram that integrates ALBI and other clinicopathological factors for predicting RFS and OS in dCCA patients. The findings of the research are likely to inform more effective treatment strategies for physicians.

Materials and methods

Patient selection

We conducted a retrospective assessment of clinical data and follow-up information from 177 patients based on specific inclusion and exclusion criteria. Inclusion criteria included: (1) patients who underwent surgery in the Department of Hepatobiliary Surgery at Beijing Chaoyang Hospital from January 2011 to January 2022; (2) preoperative imaging confirming dCCA; (3) patients who underwent radical PD or PD with allogeneic venous replacement; (4) postoperative pathology confirmed bile duct adenocarcinoma. Exclusion criteria included: (1) survival of less than one month; (2) presence of distant metastases; (3) absence of surgery; (4) multiple primary malignancies.

Data collection and follow-up

All dCCA patients received blood routine and liver function testing 3–7 days before surgery. The ALBI score was computed using the formula: ALBI = (log10 total bilirubin [μmol/L] × 0.66) + (albumin [g/L] × − 0.0852) [16]. According to the optimal cut-off value for the ALBI score, all patients were categorized into two groups: ≤ −1.67 as Low-ALBI group and > −1.67 as High-ALBI group.

Demographic data, preoperative medical records, and pathology findings were obtained. Preoperative biliary drainage was performed in selected dCCA patients based on specific clinical indications [17]. All patients received adjuvant chemotherapy postoperatively in accordance with the guidelines established by the National Comprehensive Cancer Network [18]. Postoperative follow-ups included regular radiological scans and blood testing. Any new lesion suggesting a recurrence of the initial dCCA was categorized as postoperative recurrence and diagnosed using clinical assessment, which included computed tomography, magnetic resonance imaging, and bone scintigraphy, or by pathology as appropriate. RFS was defined as the period from the original operation to the first reported recurrence and all death. Postoperative OS was calculated from the operation date to the date of death from any cause.

Ethics and informed consent

The Ethics Committee of Beijing Chao-Yang Hospital approved the study protocol (Approval No. 2020-D- 301) and waived the requirement for informed consent for the use of anonymized patient data. This study conforms to the provisions of the Declaration of Helsinki. All information was collected after obtaining written informed consent from the participants.

Statistical analysis

Continuous variables were summarized employing either the mean and standard deviation (SD) or the median and interquartile range (IQR), while categorical variables were tested using Chi-square tests or Fisher's exact tests. Kaplan–Meier curves were applied to examine survival

outcomes with log-rank testing. The Cox proportional hazards model was utilized for both univariate and multivariate studies to uncover independent prognostic variables. A significance level of $P < 0.05$ was employed. We built nomograms utilizing the independent prognostic variables. The consistency index (C-index), calibration curves, and DCA curves were applied to assess the nomogram's accuracy. Statistical analysis was performed using SPSS (IBM 22.0) and R 4.3.1 software.

Results

Associations between clinicopathological factors and the ALBI score

The study included 177 dCCA patients who experienced aggressive surgery, comprising 105 males and 72 females with an average age of 66 years. A total of 51 patients (28.8%) experienced postoperative complications. Among these complications, biochemical fistula occurred in 19 cases (10.7%), clinically relevant pancreatic fistula was observed in 13 cases (7.3%), and hemorrhage was noted in 7 cases (4.0%). Additionally, abdominal infection was present in 6 cases (3.4%), and disturbance of gastric emptying was found in 6 cases (3.4%).

Patients were classified into two groups based on the best cut-off value of the ROC curve using preoperative ALBI and the 1-year overall survival rate: the Low-ALBI group (ALBI ≤ -1.67, n = 93) and the High-ALBI group (ALBI > -1.67, n = 84). The area under the ROC curve for ALBI was 0.71, indicating a sensitivity of 60.3% and a specificity of 77.0% (Fig. 1). As demonstrated in Table 1, the preoperative albumin level was significantly greater in the Low-ALBI group, and the total bilirubin and ALBI score were significantly lower compared with the High-ALBI group. There were no significant differences between the two groups in other clinicopathological characteristics.

Correlation between the ALBI grade and survival outcomes

Among the patients included in this study, the median RFS duration was 22 months, with corresponding RFS rates of 65.6%, 38.9%, and 32.0% at 1, 3, and 5 years, respectively. The median OS duration was 26 months, with OS rates at 1, 3, and 5 years following radical surgery of 80.0%, 35.83%, and 27.5%, respectively. In the Kaplan–Meier analysis of RFS and OS based on the ALBI score, the High-ALBI group displayed significantly improved RFS and OS ($P < 0.001$) compared to the Low-ALBI

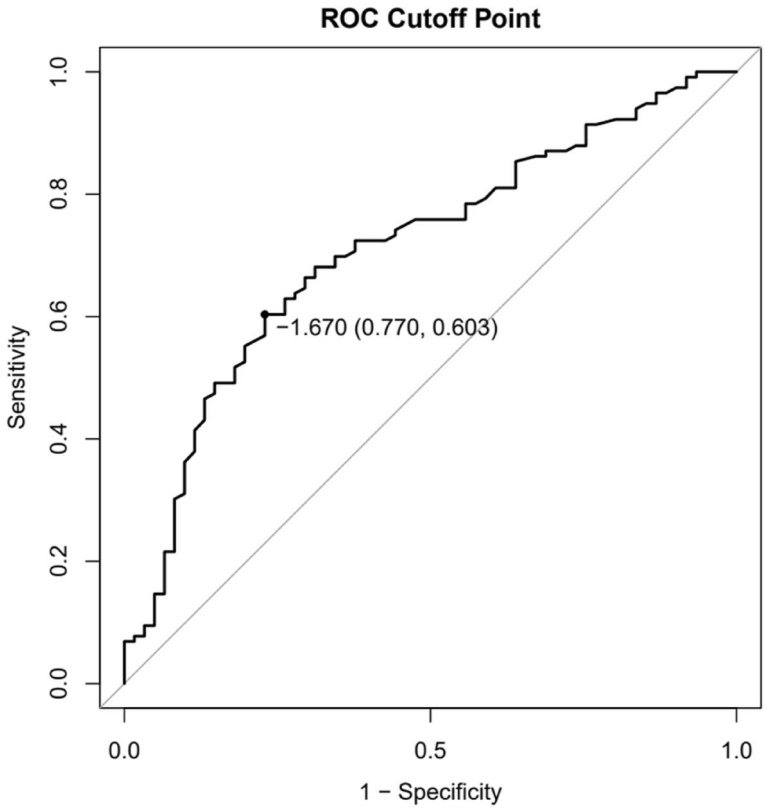

Fig. 1 ROC curves for ALBI in dCCA patients. The ROC curve using preoperative ALBI and the 1-year overall survival rate yielded an area under the curve (AUC) of 0.71 (95% CI = 0.63–0.79; $P < 0.001$), with an optimal cutoff value of − 1.67

Table 1 Demographics and clinicopathological characteristics of dCCA patients

Variables	Total (*n* = 177)	Low-ALBI (*n* = 93)	High-ALBI (*n* = 84)	P
Age, median (IQR), y	66(60,72.5)	64 (60,70.5)	67.5(60,73)	0.094
Gender, n(%)				0.799
Male	105(59.3)	56(60.2)	49(58.3)	
Female	72(40.7)	37(39.8)	35(41.7)	
BMI, mean (SD), kg/m2	23.78(3.42)	23.77(3.34)	23.78(3.52)	0.99
ALT, median (IQR), U/L	68(35.5,146.5)	66(29.5,163)	77.5(44.25,144)	0.608
TB, median (IQR), μmol/L	105.5(41.85,203.35)	49(20.55,115.55)	193.15(110.4,260.78)	< 0.001
Albumin, mean (SD), g/L	35.51(5.88)	39.52(3.81)	31.08(4.39)	< 0.001
ALBI score, mean (SD)	− 1.75(0.67)	− 2.27(0.41)	− 1.18(0.37)	< 0.001
CA19 - 9, median (IQR), U/mL	68(26,245.85)	59.2(23.65,205.1)	75.5(28.6,381.83)	0.146
CEA, median (IQR), U/mL	2(1.2,3.15)	1.8(1.2,3.2)	2.15(1.23,3.15)	0.542
Biliary drainage, n(%)				0.732
Yes	84(47.5)	43(46.2)	41(48.8)	
No	93(52.5)	50(53.8)	43(51.2)	
Biliary drainage duration, mean (SD), days	7.82(0.83)	7.85(1.23)	7.80(1.11)	0.849
Degree of differentiation, n(%)				0.682
Poor	60(33.9)	30(32.3)	30(35.7)	
Moderate-Well	117(66.1)	63(67.7)	54(64.3)	
Tumor size, median (IQR), cm	2(1.5,2.5)	2(1.5,2.5)	2(1.5,2.5)	0.693
Resection margin, n(%)				0.883
R0	169(95.5)	89(95.7)	80(95.2)	
R1	8(4.5)	4(4.3)	4(4.8)	
Portal vein invasion, n(%)				0.167
Yes	23(13)	9(9.7)	14(16.7)	
No	154(87)	84(90.3)	70(83.3)	
Lymph node invasion, n(%)				0.128
Yes	80(45.2)	37(39.8)	43(51.2)	
No	97 (54.8)	56(60.2)	41(48.8)	
Postoperative chemotherapy, n(%)				0.705
Yes	53(29.9)	29(31.2)	24(28.6)	
No	124(70.1)	64(68.8)	60(71.4)	

group. The median RFS for patients in the High-ALBI and Low-ALBI groups was 14 and 50 months, with corresponding 1-, 3-, and 5-year RFS rates of 55.8%, 23.5%, 11.7%, and 74.2%, 52.1%, 48.4%, respectively (Fig. 2A). The median OS in the two groups was 18 and 38 months, with 1-, 3-, and 5-year OS rates of 68.6%, 20.3%, 10.1%, and 90.2%, 50.1%, 43.1%, respectively (Fig. 2B).

Univariate and multivariate analysis of prognostic factors for RFS and OS

In univariate Cox regression, albumin, total bilirubin, ALBI, CA19 - 9, degree of differentiation, lymph node invasion, and portal vein invasion were significant for RFS and OS (P < 0.05). In the multivariate Cox regression of OS, the ALBI (HR: 2.091; 95%CI: 1.294–3.377; P = 0.003), CA19 - 9(HR: 1.655; 95%CI: 1.067–2.569; P = 0.025), degree of differentiation(HR: 1.556; 95%CI: 1.047–2.312; P = 0.029), lymph node invasion (HR: 2.312; 95%CI: 1.562–3.421; P < 0.001), and portal vein invasion (HR: 2.182; 95%CI: 1.293–3.683; P = 0.003) were independent prognostic factors (Table 2). In the multivariate Cox regression of RFS, the ALBI (HR: 2.073; 95%CI: 1.261–3.408; P = 0.004), degree of differentiation(HR: 1.597; 95%CI: 1.056–2.415; P = 0.027), lymph node invasion (HR: 2.700; 95%CI: 1.791–4.070; P < 0.001), and portal vein invasion (HR: 1.800; 95%CI: 1.035–3.128; P = 0.037) were independent prognostic factors (Table 3).

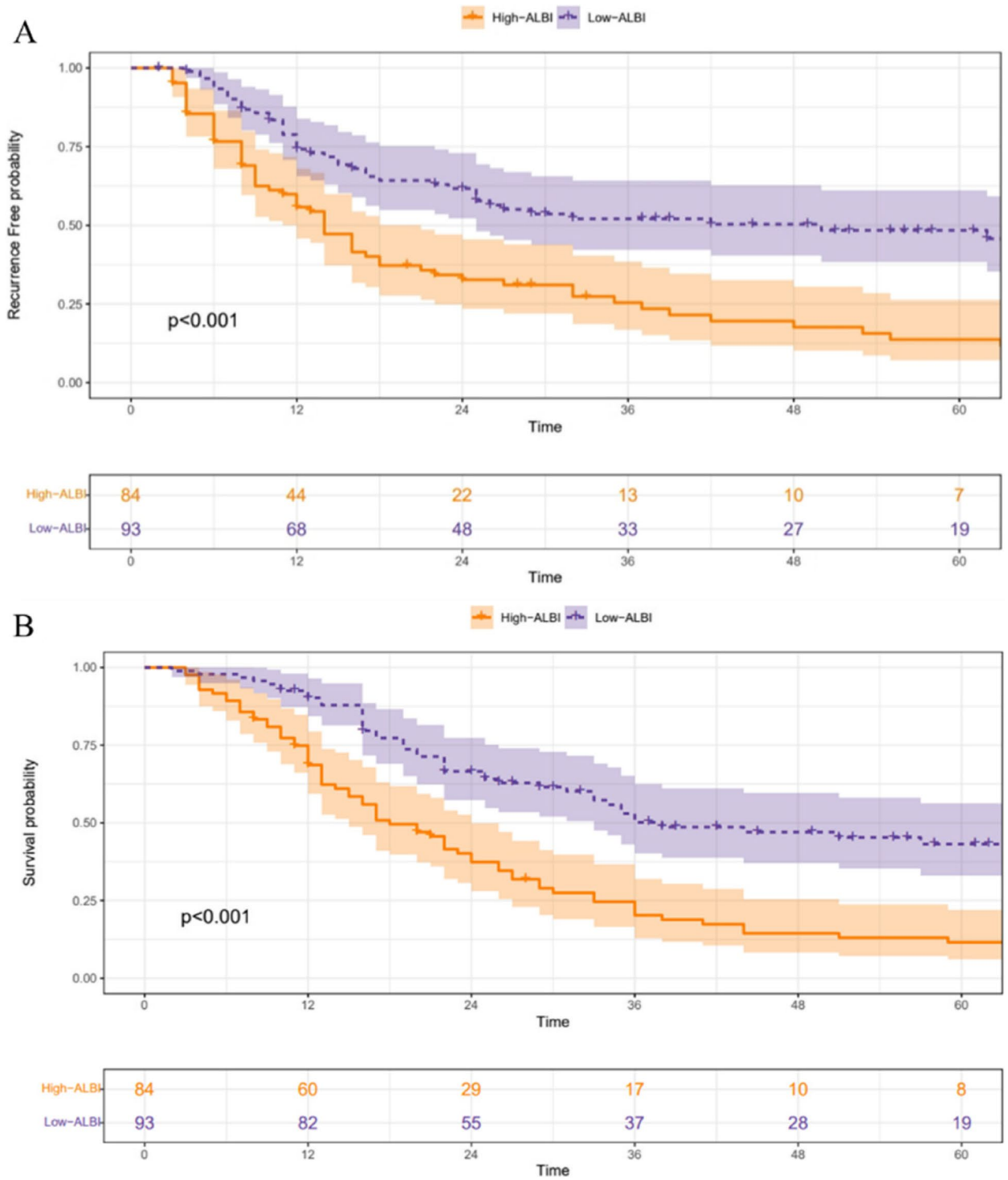

Fig. 2 Kaplan–Meier survival curves for RFS and OS in dCCA patients. **A** Median RFS times in the High-ALBI and Low-ALBI groups were 14 and 50 months, respectively ($P < 0.001$). **B** Median OS times in the High-ALBI and Low-ALBI groups were 18 and 38 months, respectively ($P < 0.001$)

Construction of the prognostic nomogram

Using a multivariable COX regression analysis, we developed nomograms for predicting 1-year, 3-year, and 5-year RFS and OS in dCCA patients (Fig. 3A-B). The RFS nomogram has a C-index value of 0.74, while the OS nomogram's C-index value is 0.75, suggesting

Table 2 Univariable and multivariable analysis of the prognostic factors for RFS

Variable	N	Univariate Analysis		Multivariate Analysis	
		HR(95% CI)	*p* Value	HR(95% CI)	*p* Value
Gender					
Female	72	Reference	0.868		
Male	105	1.033(0.702–1.521)			
Age (y)					
< 60	41	Reference	0.936		
≥ 60	136	0.982(0.613–1.528)			
Albumin (g/L)					
≥ 40	38	Reference	0.042	Reference	0.970
< 40	139	1.676(1.019–2.754)		1.011(0.559–1.830)	
Total bilirubin (μmol/L)					
≤ 26	33	Reference	0.034	Reference	0.849
> 26	144	1.732(1.042–2.878)		0.849(0.460–1.564)	
ALBI					
< – 1.67	93	Reference	< 0.001	Reference	0.004
≥ – 1.67	84	2.208(1.504–3.243)		2.073(1.261–3.408)	
CA19 - 9 (U/ml)					
< 37	58	Reference	0.007	Reference	0.086
≥ 37	119	1.776(1.167–2.703)		1.471(0.947–2.284)	
ALT(U/L)					
≤ 40	66	Reference	0.498		
> 40	111	1.145(0.773–1.697)			
CEA (U/ml)					
< 5	160	Reference	0.076		
≥ 5	17	1.666(0.948–2.926)			
Degree of differentiation					
Moderate-Well	117	Reference	0.001	Reference	0.027
Poor	60	1.934(1.307–2.862)		1.597(1.056–2.415)	
Tumor size (cm)					
< 3	142	Reference	0.138		
≥ 3	35	1.419(0.893–2.253)			
Resection margin					
R0	169	Reference	0.806		
R1	8	1.119(0.456–2.750)			
Lymph node invasion					
No	97	Reference	< 0.001	Reference	< 0.001
Yes	80	3.258(2.190–4.828)		2.700(1.791–4.070)	
Portal vein invasion					
No	154	Reference	< 0.001	Reference	0.037
Yes	23	2.753(1.605–4.720)		1.800(1.035–3.128)	
Postoperative chemotherapy					
Yes	124	Reference	0.920		
No	53	0.979(0.650–1.475)			

their accurate prognostic prediction capability. Calibration curves indicate that the predictions of the 5-year survival probability models for RFS and OS closely correspond with the actual observations (Fig. 4A-B). Furthermore, DCA curves were built to test the prediction ability of the nomograms in comparison to the AJCC TNM stage. The results demonstrated a significantly greater benefit from our model compared to the

Table 3 Univariable and multivariable analysis of the prognostic factors for OS

Variable	N	Univariate Analysis		Multivariate Analysis	
		HR(95% CI)	*p* Value	HR(95% CI)	*p* Value
Gender					
Female	72	Reference	0.729		
Male	105	1.068(0.735–1.553)			
Age (y)					
< 60	41	Reference	0.653		
≥ 60	136	1.105(0.714–1.711)			
Albumin (g/L)					
≥ 40	38	Reference	0.005	Reference	0.542
< 40	139	2.103(1.256–3.523)		1.206(0.660–2.206)	
Total bilirubin (μmol/L)					
≤ 26	33	Reference	0.005	Reference	0.863
> 26	144	2.104(1.256–3.525)		0.947(0.509–1.760)	
ALBI					
< – 1.67	93	Reference	< 0.001	Reference	0.003
≥ – 1.67	84	2.532(1.741–3.683)		2.091(1.294–3.377)	
CA19 - 9 (U/ml)					
< 37	58	Reference	< 0.001	Reference	0.025
≥ 37	119	2.158(1.420–3.279)		1.665(1.067–2.569)	
ALT(U/L)					
≤ 40	66	Reference	0.407		
> 40	111	1.175(0.803–1.719)			
CEA (U/ml)					
< 5	160	Reference	0.296		
≥ 5	17	1.348(0.770–2.359)			
Degree of differentiation					
Moderate-Well	117	Reference	< 0.001	Reference	0.029
Poor	60	1.961(1.348–2.852)		1.556(1.047–2.312)	
Tumor size (cm)					
< 3	142	Reference	0.070		
≥ 3	35	1.499(0.968–2.322)			
Resection margin					
R0	169	Reference	0.855		
R1	8	1.087(0.444–2.665)			
Lymph node invasion					
No	97	Reference	< 0.001	Reference	< 0.001
Yes	80	2.792(1.914–4.072)		2.312(1.562–3.421)	
Portal vein invasion					
No	154	Reference	< 0.001	Reference	0.003
Yes	23	3.214(1.927–5.359)		2.182(1.293–3.683)	
Postoperative chemotherapy					
Yes	124	Reference	0.300		
No	53	1.246(0.822–1.889)			

TNM stage (Fig. 4C-D). Each factor was assigned points based on the nomogram, and the total points were calculated by summing the assigned points for all factors. Patients were classified into low-point and high-point groups according to specified cutoff values in the RFS and OS nomograms (215.4 and 262.3, respectively). Kaplan–Meier survival curves (Fig. 5A-B) demonstrated that patients in the high-point group exhibited markedly superior prognoses compared to those in the low-point group ($p < 0.001$).

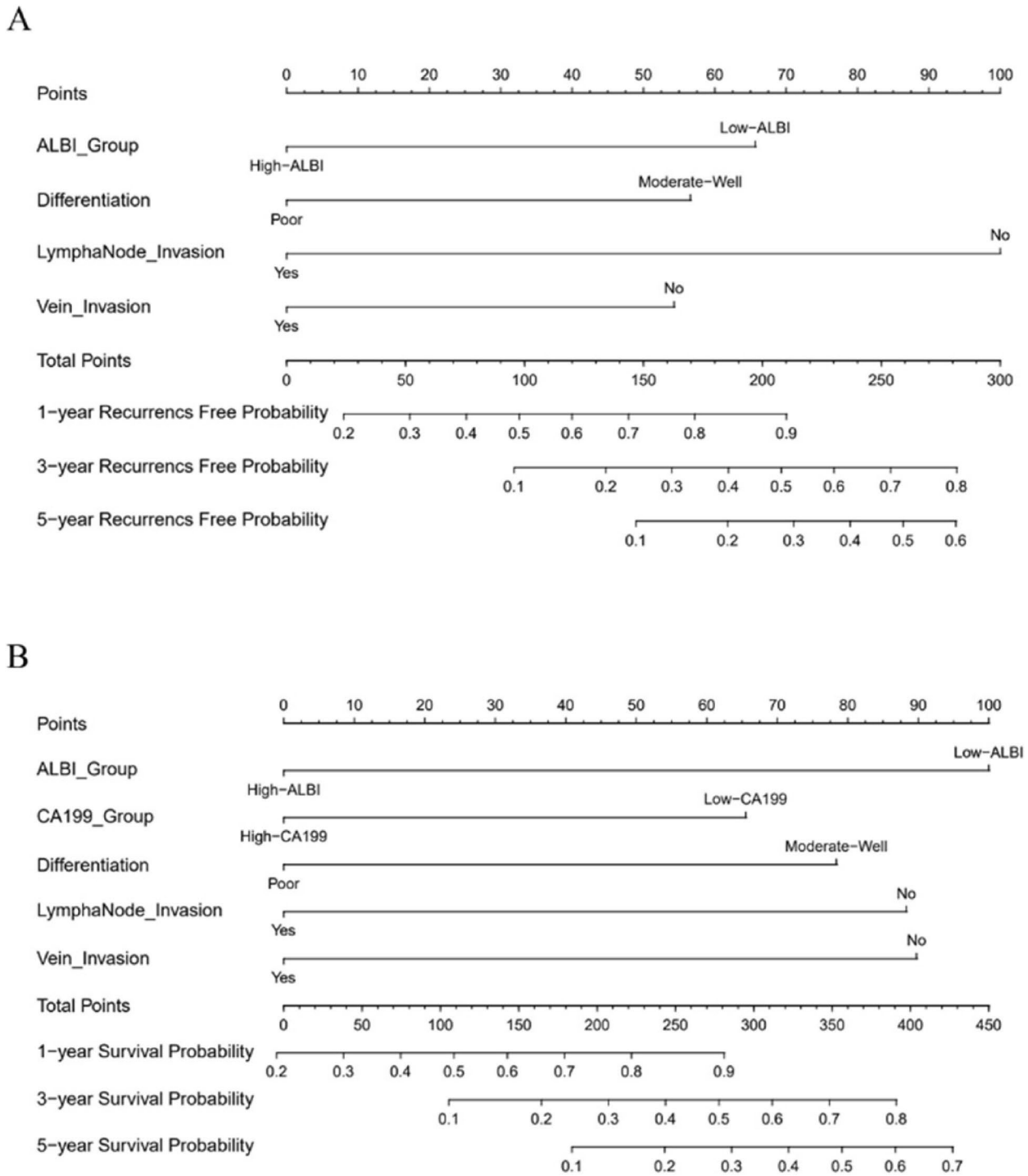

Fig. 3 Nomograms developed based on multivariate Cox analysis. **A** Nomogram for predicting RFS in dCCA patients. **B** Nomogram for predicting OS in dCCA patients

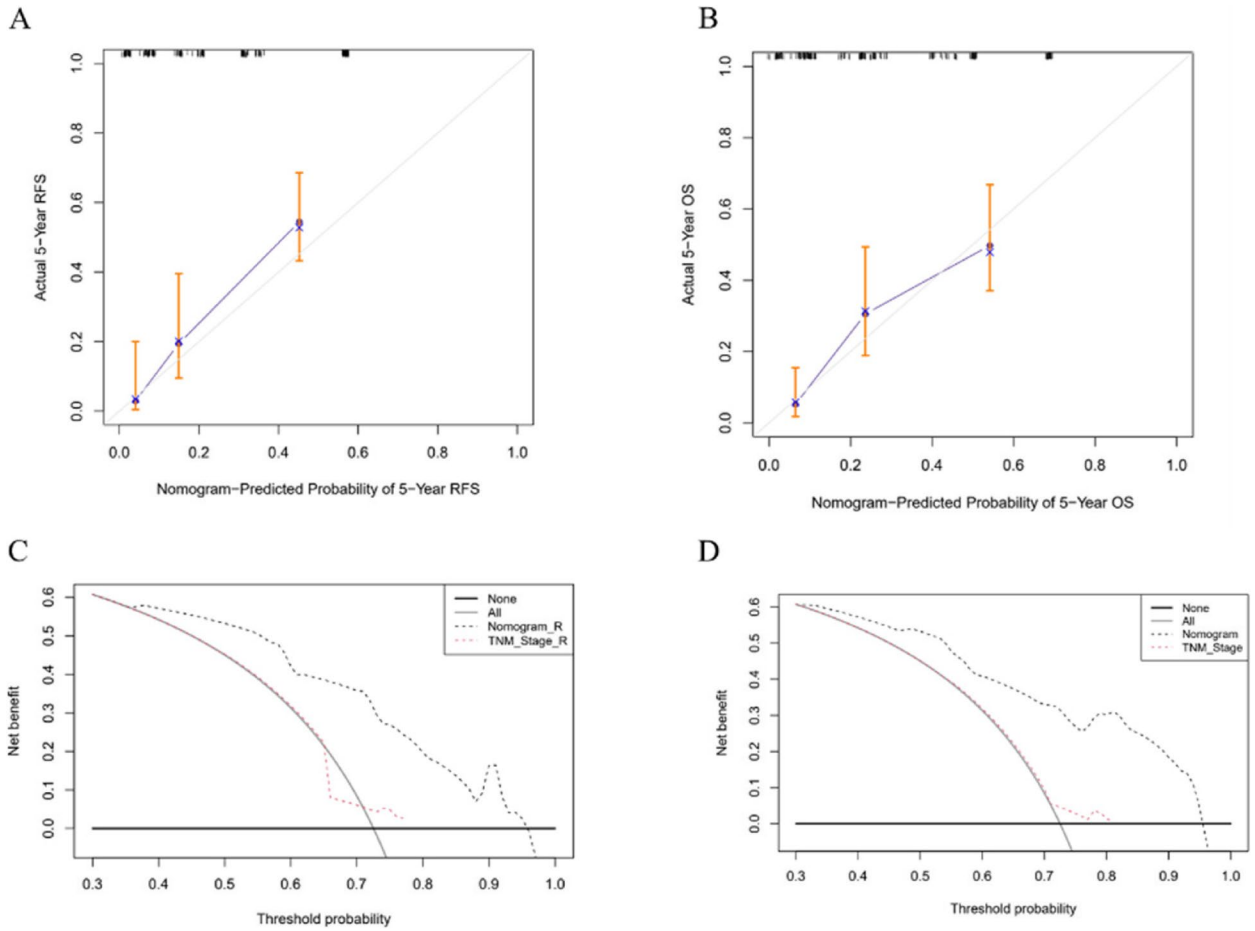

Fig. 4 Development of the nomograms for dCCA patients. **A** Calibration curve for 5-year RFS. **B** Calibration curve for 5-year OS. **C** Decision curve analysis (DCA) curve for 5-year RFS. **D** DCA curve for 5-year OS

Discussion

As a malignant tumor emerging from the epithelium distal to the insertion of the cystic duct, dCCA may rapidly infiltrate the biliary tree in a short period, and it's crucial to treat with dCCA in an early stage [19]. With the advancement of chemotherapy and radiology, radical surgery remains the foundation of curative therapy for dCCA. The surgical excision of dCCA typically involves a pancreaticoduodenectomy and lymphadenectomy of nodes surrounding the common bile duct and porta hepatis [20]. In a large cohort of cholangiocarcinoma patients who had surgical resection, 78% of those with dCCA achieved R0 resection [21]. In addition to surgical details, the preoperative nutritional status and pathological findings significantly impact postoperative complications and the survival outcomes of patients with dCCA after surgery [22].

Due to the anatomical location of the primary tumor, the majority of advanced-stage dCCA patients present at the hospital with obstructive jaundice in a malnourished state. Furthermore, surgery causes an inflammatory response corresponding with the level of surgical trauma, prompting a metabolic stress response. Preoperative nutritional assessment plays a vital role in advising physicians to establish appropriate treatment regimens. While some research has explored some nutritional evaluation tools in dCCA [23–25], the effect of ALBI in dCCA still needs more evaluation.

ALBI, a novel nutritional status scoring system, is derived from the values of albumin and total bilirubin. ALBI has a great effect on the prognosis of some malignant tumors [26–28]. The result above with in consistent with our study, low-ALBI was an independent prognostic factor in predicting the OS of dCCA patients. Additionally, we observed that patients in Low-ALBI group have a much longer RFS.

As a part of ALBI, albumin was usually defined as a simple yet efficient indication for reflecting the body's nutritional state, which plays a key role in cancer cell immunological responses. Previous studies have

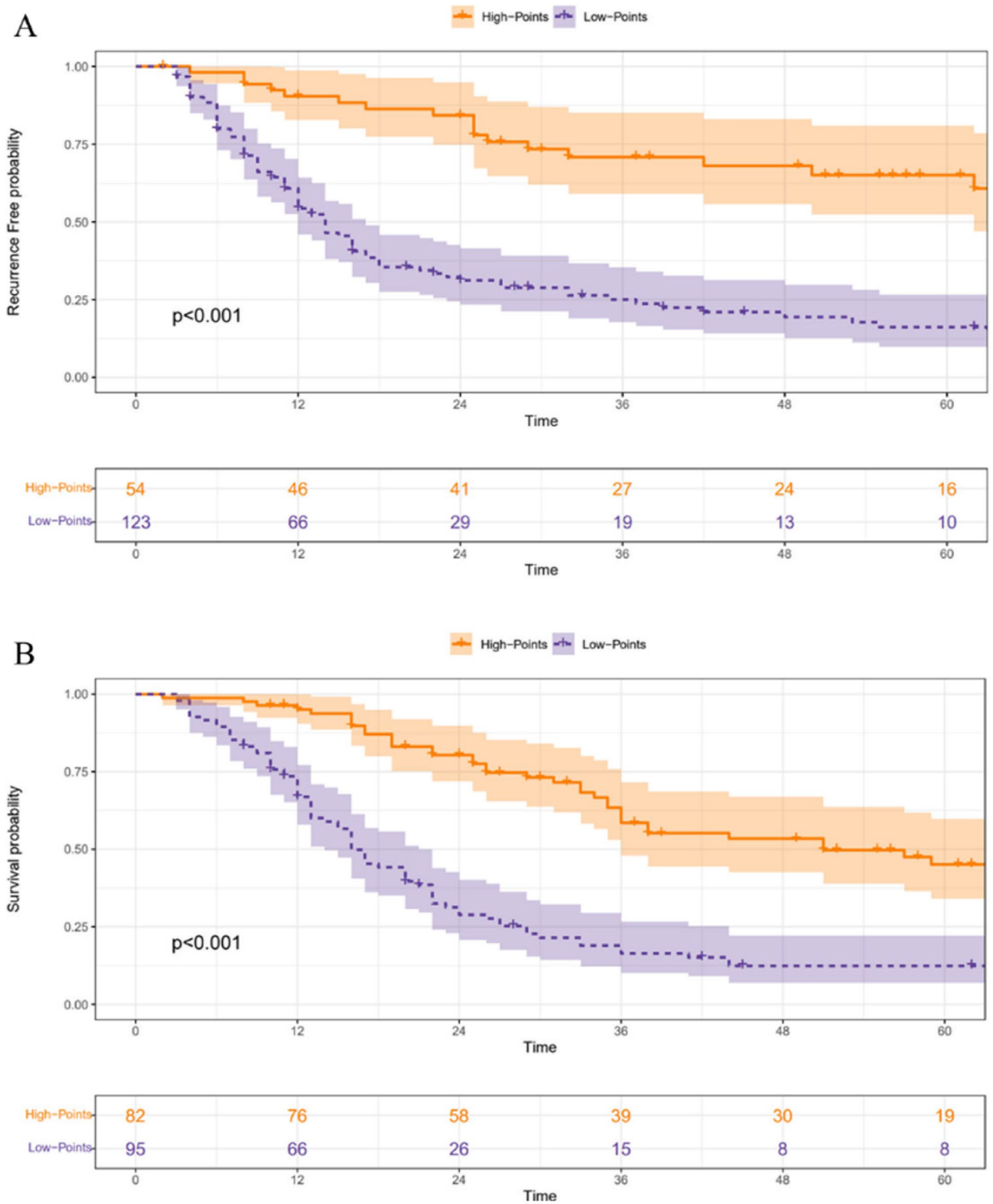

Fig. 5 Kaplan–Meier survival curves for risk groups. **A** Kaplan–Meier survival curve for RFS in high-point and low-point groups. **B** Kaplan–Meier survival curve for OS in high-point and low-point groups

consistently identified serum albumin as a significant prognostic factor in a wide range of malignancies [29, 30]. Furthermore, hypoalbuminemia impairs the systemic immune system while boosting tumor cell growth. Research has demonstrated that reduced serum albumin levels may be induced by pro-inflammatory cytokines, which affect albumin synthesis by hepatocytes [31, 32]. Numerous studies have indicated that low preoperative serum albumin levels are linked to poor OS in patients with intrahepatic and perihilar cholangiocarcinoma [33, 34]. The univariate analysis of albumin in our study also indicates the potential predictive ability of OS and RFS in dCCA.

Hyperbilirubinemia was associated with dysfunction of the liver, kidneys, and immune system, and heightened gut mucosa permeability [35]. Recent studies have indicated a significant correlation between low serum bilirubin levels following biliary drainage and reduced mortality rates [36, 37]. However, despite performing preoperative biliary drainage to reduce total bilirubin levels, full liver function recovery may take 4–6 weeks. From the univariate analysis of our study, a high level of total bilirubin may have a negative effect on the prognosis of dCCA. A retrospective study analyzing 115 perihilar cholangiocarcinoma patients arrived at a similar conclusion. Patients with low preoperative bilirubin levels exhibited significantly superior OS and RFS rates compared to patients with high preoperative bilirubin levels [38].

Apart from the ALBI reflecting the nutritional status of dCCA patients, CA19 - 9 and tumor differentiation represent tumor malignancy from some perspective. Some previous studies have found a relationship between CA19 - 9 and the survival of dCCA [39, 40]. Patients who had poor differentiation tend to have poor overall survival and early recurrence [41–43]. Besides, the invasion of the portal vein and lymph node also reflects the malignancy of the tumor and results in a poor prognosis in dCCA patients [44, 45]. We must consider all these nutritional and oncological factors in predicting survival in a more accurate method.

Nomograms have been developed and demonstrated superior accuracy compared to conventional staging systems in predicting prognosis for certain cancers [46, 47]. Therefore, we constructed a prognostic nomogram that integrates nutritional status and oncological factors for patients with dCCA following radical surgery. The nomogram exhibited strong predictive performance for survival, which was verified by the C-index and calibration curve. Comparing the nomogram to the AJCC staging system revealed that the nomogram exhibited superior predictive accuracy and greater clinical utility. Using the scores predicted by the nomogram, patients could be categorized into two groups. The Kaplan–Meier data revealed significant differences in RFS and OS between these two groups. Given the dismal prognosis of the low-points group, patients in this category should receive heightened care. The nomogram can enable clinicians in early prognosis evaluation, guide adjuvant treatment options, and stratify patients based on the anticipated risk score.

The research has several limitations that should be addressed in future research. First, the relatively small sample size from a single-center cohort may limit the generalizability and accuracy of our findings. The results might not fully reflect the broader population of dCCA patients, and larger, multi-center studies are needed to validate these conclusions. Second, due to the limited sample size, we were unable to conduct both internal and external validation of the nomograms. This step is crucial to ensure the robustness and applicability of the predictive model across diverse patient populations. In future studies, we aspire to validate the ALBI score in diverse patient cohorts and utilize these findings to guide the design of future clinical trials.

Conclusion

In conclusion, ALBI was an independent prognostic factor in predicting RFS and OS of dCCA patients after radical surgery. The nomograms based on ALBI can provide reliable, personalized survival prediction for patients with dCCA following radical surgery.

Acknowledgements
None.

Authors' contributions
JC Huang and YW Ma drafted the manuscript and performed the statistical analysis; HX Wang searched articles and collected the data; RL and TJ designed, revised, and guided this study. All authors have read and approved the final manuscript.

Funding
None.

Data availability
All data generated or analyzed during this study are included in this article.

Declarations

Ethics approval and consent to participate
This study was conducted in accordance with the Declaration of Helsinki (as revised in 2013). The study was approved by the Ethics Committee of Beijing Chao-Yang Hospital (No. 2020-D- 301) and individual consent for this retrospective analysis was waived.

Competing interests
The authors declare no competing interests.

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Received: 4 February 2025 Accepted: 14 April 2025
Published online: 24 April 2025

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