CANCER DIAGNOSIS & PROGNOSIS 6: 703-714 (2026)
doi: 10.21873/cdp.10570

Prognosis Using Modified Albumin–Bilirubin Grade in Resected Biliary Tract Cancer: A Multicenter Propensity Score–matched Analysis

TORU TAKAHASHI[1], HIROAKI YANAGIMOTO[1], MASAYUKI AKITA[1], DAISUKE TSUGAWA[1], MICHIHIKO YOSHIDA[1], YASUHIRO UEDA[2], TARO OKAZAKI[2], KIMIHIKO UENO[3], HAYATO MIYAZAKI[4], IZURU OTSUBO[4], SHOHEI KOMATSU[1] and TAKUMI FUKUMOTO[1]

[1]Department of Surgery, Division of Hepato-Biliary-Pancreatic Surgery, Kobe University Graduate School of Medicine, Kobe, Japan;
[2]Division of Gastroenterological Surgery, Hyogo Cancer Center, Hyogo, Japan;
[3]Department of Surgery, National Hospital Organization Kobe Medical Center, Hyogo, Japan;
[4]Department of Surgery, Akashi Medical Center, Hyogo, Japan

Abstract

Background/Aim: Currently, the modified albumin-bilirubin (mALBI) grade, a novel liver function assessment, is used as a prognostic factor in many areas of gastrointestinal cancer. We evaluated whether mALBI grade predicted survival in a large multicenter cohort of patients who underwent curative-intent resection for biliary tract cancer (BTC).

Patients and Methods: We retrospectively analyzed data for 634 patients who underwent curative resection for BTC at four centers during 2001-2023. The mALBI grade was calculated from preoperative albumin and total bilirubin levels. Cox proportional hazards regression was used to assess the association of mALBI grade with overall survival (OS) and recurrence-free survival (RFS) in a propensity score-matched cohort. The mALBI grade was defined by subdividing ALBI grade 2 at a cutoff of −2.27; patients with mALBI grades 1-2a were classified as the low mALBI group, and those with grades 2b-3 as the high mALBI group.

Results: After propensity score-matching, the high mALBI group remained associated with poorer OS (44 *vs*. 70 months; p=0.015) than the low mALBI group. Multivariate analysis revealed that high mALBI grade was independently associated with poor OS (hazard ratio=1.584, 95% confidence interval=1.077-2.331; p=0.020) and RFS (hazard ratio =1.447, 95% confidence interval=1.023-2.046, p=0.037).

Conclusion: A high mALBI grade was associated with shorter OS and RFS in patients with resected BTC. Preoperative mALBI grade is an important prognostic indicator for risk stratification and prognostic evaluation.

Keywords: Modified albumin-bilirubin grade, biliary tract cancer, multicenter study, overall survival, adjunctive therapy.

✉ Hiroaki Yanagimoto, MD, PhD, Department of Surgery, Division of Hepato-Biliary-Pancreatic Surgery, Kobe University Graduate School of Medicine, 7-5-2 Kusunoki-cho, Chuo-ku, Kobe 650-0017, Japan. Tel: +81 783826302, Fax: +81 783826307, e-mail: yanagimh@med.kobe-u.ac.jp

Received March 25, 2026 | Revised April 30, 2026 | Accepted May 5, 2026

Introduction

Biliary tract cancer (BTC) is an invasive adenocarcinoma that can originate from the bile ducts, gallbladder, or ampulla of Vater, and has a poor prognosis (1). It is the second most common hepatobiliary cancer worldwide, with high incidence rates in the Asia-Pacific region and South America (2, 3). Complete surgical resection is the only curative treatment for BTC (4). Despite recent advancement in surgical techniques, perioperative management, and postoperative treatment, the long-term prognosis of surgically treated patients is unsatisfactory (5, 6). Long-term cure is achievable only in patients with early-stage tumors that are amenable to resection (7). However, a large-scale clinical trial demonstrated that disease recurrence occurred in 60% of cases after tumor resection resulting in a 5-year survival rate of under 50%, even among patients administered adjuvant chemotherapy (7). Therefore, great efforts are being made to improve early diagnosis and multimodal treatment including chemotherapy, for better outcomes (6, 8). The survival of patients with BTC is affected by several factors including tumor-node-metastasis stage (9), neurovascular invasion, tumor differentiation, and resection margin status, which are typically assessed intraoperatively.

Recently, a novel liver function assessment model, the albumin–bilirubin (ALBI) grade, was introduced (10). This straightforward model is derived from serum albumin and total bilirubin levels obtained from routine blood tests and has gained attention as a noninvasive index for evaluating liver function. The ALBI grade outperforms the Child–Pugh grade in assessment of liver function, predicting complications, and estimating prognosis in liver disease (11, 12). Another study showed that the modified ALBI (mALBI) grade, which subdivides patients by conventional ALBI score, offers improved accuracy for assessment of liver function and enhanced utility in stratifying patient prognosis (13). A growing body of literature has demonstrated the prognostic relevance of the ALBI score across a wide spectrum of malignancies extending beyond BTC (14-17). However, to the best of our knowledge, the mALBI score has not been investigated in a multicenter case series involving patients after resection of BTC. The purpose of this multicenter study was to evaluate the prognostic utility of the mALBI score in such patients.

Patients and Methods

Study design. Patients with histologically confirmed perihilar cholangiocarcinoma (PHCC), distal cholangiocarcinoma (DCC), gallbladder carcinoma (GBC), ampullary carcinoma (AC), or intrahepatic cholangiocarcinoma (ICC), diagnosed based on surgically resected specimens, were retrospectively enrolled in this study at four centers between 2001 and 2023. These patients were observed until the follow-up cutoff date (December 2023) or death following surgical resection. Clinicopathological data were obtained from the medical records. Collected clinical data included sex, age, tumor location, presence of preoperative cholangitis, preoperative laboratory parameters (albumin and total bilirubin), and tumor markers [including carcinoembryonic antigen and carbohydrate antigen (CA19-9)], surgical details (type of surgery, operative time, intraoperative blood loss, and concomitant major vascular resection and reconstruction), postoperative hospital stay, postoperative complications, details of adjuvant chemotherapy, recurrence, survival, and pathological findings (tumor differentiation, pathological T factor, lymph node metastasis, lymphatic, vascular, and perineural invasion, and residual tumor status). Pathological findings were classified according to the seventh edition of the Union for International Cancer Control TNM staging system (18). Preoperative cholangitis was diagnosed according to the criteria outlined in the 2018 Tokyo guidelines (19). Postoperative complications were classified according to the Clavien–Dindo classification system (20). Major complications were defined as grade ≥3. This study was approved by the Ethics Committee of Kobe University (approval ID: B240209) and other centers and was conducted in accordance with the Declaration of Helsinki (2024). Informed consent was obtained from all participants using an opt-out approach.

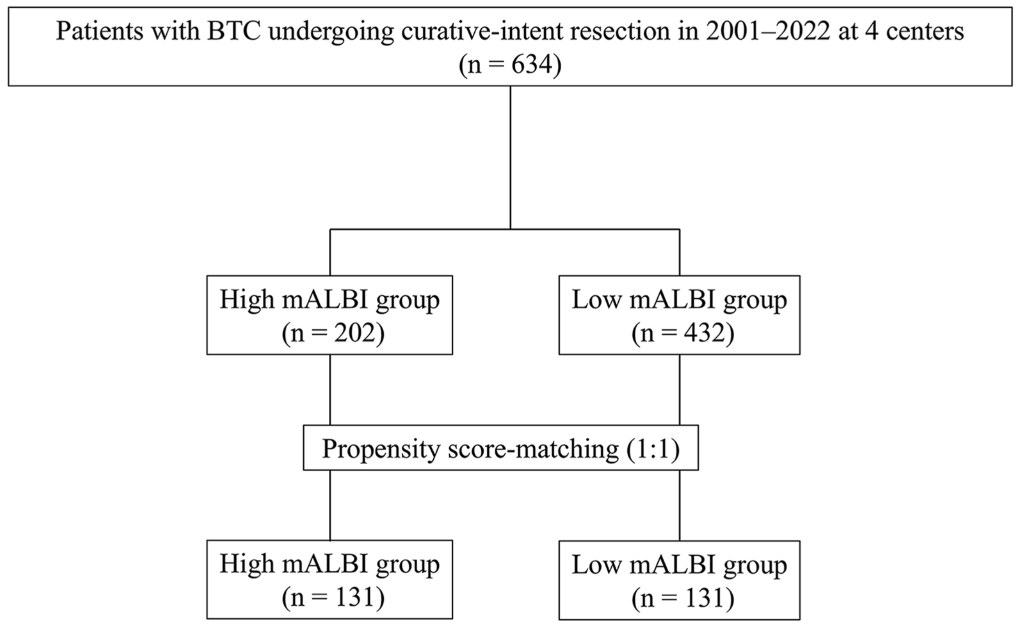


Figure 1. *Flow diagram of patient selection and propensity score-matching. A total of 634 patients with biliary tract cancer (BTC) who underwent radical resection between 2001 and 2022 at four centers were included. Patients were classified into groups with high (n=202) or low (n=432) modified albumin–bilirubin (mALBI) score. After 1:1 propensity score-matching, 131 patients were included in each group. Matching variables included age, sex, preoperative cholangitis, carbohydrate antigen 19-9, tumor T and N categories, lymphatic invasion, vascular invasion, and R category.*

mALBI score. The ALBI score was defined as follows: ($\log_{10}$total bilirubin × 0.66) + (albumin × -0.085) with total bilirubin (μmol/l) and albumin (g/l) determined preoperatively. ALBI grades were then categorized as grade 1 for scores ≤−2.60, grade 2 for scores >−2.60 to −1.39, and grade 3 for scores >−1.39. Consistent with previous studies, ALBI grade 2 was further subdivided using a cut-off value of −2.27 into grades 2a (−2.60≤ ALBI score <−2.27) and 2b (−2.27≤ ALBI score <−1.39) (13). For this study, we defined patients with mALBI grades 1 and 2a as the low mALBI group, and those with grades 2b and 3 as the high mALBI group.

Statistical analysis. Descriptive statistics are presented as medians with ranges for continuous variables, and as numerical values with percentages for categorical variables. Continuous variables were compared using the Kruskal–Wallis test, whereas categorical variables were analyzed using Pearson's chi-square test or Fisher's exact test. OS was defined as the interval from the date of surgery to the date of death from any cause or last follow-up. Recurrence-free survival (RFS) was defined as the interval between surgery and relapse, death, or the last follow-up. Kaplan–Meier survival curves were used to estimate OS and RFS, and the differences between the curves were assessed using the log-rank test. Univariate analysis was conducted to identify potential risk factors for OS and RFS. Variables with a value p<0.10 in the univariate analysis, along with clinically relevant factors were included in a multivariate Cox proportional hazards model to identify factors independently associated with postoperative survival. The results were reported as hazard ratios (HRs) with 95% confidence intervals (CIs). Statistical significance was set at p<0.05. All statistical analyses were performed using JMP statistical software version 18 (SAS Institute Inc., Cary, NC, USA).

PSM analysis. PSM was used to balance patient characteristics between the high and low mALBI groups. The matching algorithm used was nearest-neighbor matching with a 1:1 ratio, and the caliper was set to 0.02. The variables age group, sex, tumor location, preoperative cholangitis, CA19-9, T category, N category, vascular invasion, lymphatic invasion, perineural invasion, and R category were matched.

Ethics statement. This study was approved by the Ethics Committee of Kobe University (approval ID: B240207) and was conducted in accordance with the principles of the Declaration of Helsinki (2024). Informed consent was obtained from all participants using an opt-out approach in which patients were given the opportunity to decline participation after being informed about the study.

Results

Characteristics of patients and assessment of efficacy. The initial cohort comprised 716 patients. After excluding patients with distant metastases (M1) (n=28), macroscopic residual cancer after resection (R2) (n=28), double cancer (n=22), and those lost to follow-up (n=4), 634 patients were enrolled in the study (Figure 1). The baseline data of these patients are presented in Table I.

A total of 108 (17%) patients were clinically or pathologically diagnosed with PHCC, 155 (24%) with DCC, 140 (22%) with GBC, 140 (22%) with AC, and 90 (14%) with ICC. The patients had a median age of 71 years (range=25-89 years) and 382 (60%) were men. According to mALBI grade, 202 (32%) patients were in the high mALBI group, and 432 (68%) were in the low mALBI group. Pancreaticoduodenectomy was most commonly performed (n=306, 48%), followed by hepatectomy (n=202, 31.9%), and gallbladder bed resection (n=82, 13%). A total of 23 (4%) patients underwent concomitant portal vein resection and reconstruction (PVR), and 6 (1%) others underwent concomitant hepatic artery resection and reconstruction. Microscopic residual cancer was observed in the resection margins in 104 patients (16.4%). A total of 165 (26.0%) patients were administered adjuvant chemotherapy after surgical resection. After 1:1 PSM, the high mALBI group (n=131) was compared with the low mALBI group (n=131) having balanced baseline characteristics (Table I).

Associations between mALBI grade and clinical variables after PSM. The clinicopathological characteristics of patients according to mALBI are shown in Table I. No significant differences in sex, age, body mass index, tumor location, carcinoembryonic antigen, CA19-9, PVR, hepatic artery resection and reconstruction, operative time, intraoperative blood loss, postoperative complications, major complications, adjuvant chemotherapy, or any of the pathological characteristics were observed between the groups. Although the high mALBI group had a significantly longer postoperative hospital stay (p=0.045), there were no significant differences in the incidence of major postoperative complications (p=0.922).

OS. The median duration of follow-up for the whole cohort was 94 months. Patients in the high mALBI group (n=202) had significantly worse prognosis in terms of OS than those in the low mALBI group (n=432) (median=39 *vs.* 164 months; p<0.001) (Figure 2A, upper panel). After PSM, the high mALBI group (n=131) had a significantly worse prognosis in terms of OS than the low mALBI group (n=131) (median=44 *vs.* 70 months; p=0.015) (Figure 2B, upper panel).

In analyses stratified by tumor location, patients in the high mALBI group consistently demonstrated significantly worse OS than those in the low mALBI group across all tumor sites. In extrahepatic cholangiocarcinoma, the median OS was 35 months for the high mALBI group (n=133) and 61 months for the low mALBI group (n=130) (p=0.007). In GBC, the median OS was 50 months (n=24) *versus* 165 months (n=116), respectively (p=0.013). Among patients with AC, the median OS was 69 months for the high mALBI group (n=35), whereas it was not achieved for the low mALBI group (n=105) (p<0.001). Similarly, in ICC, the median OS was 39 months for the high mALBI group (n=9) and was not achieved for the low mALBI group (n=81) (p=0.039) (Figure 3).

Patients were further categorized according to surgical procedure into a hepatectomy and non-hepatectomy

Table I. *Comparison of clinicopathological characteristics by modified albumin-bilirubin (mALBI) group before (overall cohort) and after propensity score-matching.*

		Overall cohort, n (%)			Matched cohort, n (%)		
Variable	Subgroup	High mALBI (n=202)	Low mALBI (n=432)	*p*-Value	High mALBI (n=131)	Low mALBI (n=131)	*p*-Value
Sex	Male	127 (63.2)	255 (59.0)	0.319	78 (59.5)	78 (59.5)	1.000
Age	≥70 Years	125 (62.2)	235 (54.4)	0.065	76 (58.0)	84 (64.1)	0.311
BMI	≥25 kg/m^2	27 (14.4)	107 (25.7)	**0.002**	21 (16.9)	27 (21.3)	0.384
Preoperative cholangitis	Yes	119 (63.0)	70 (16.6)	**<0.001**	58 (44.3)	51 (46.8)	0.380
Tumor type	PHCC	55 (27.4)	53 (12.3)		33 (25.2)	28 (21.4)	0.305
	DCC	78 (38.8)	77 (17.8)		52 (38.5)	43 (31.9)	
	GBC	24 (11.9)	116 (26.9)		18 (13.7)	31 (23.7)	
	AC	35 (17.4)	105 (24.3)		24 (18.3)	24 (18.3)	
	ICC	9 (4.5)	81 (18.8)		7 (5.3)	8 (6.1)	
CEA	>5.0 ng/ml	32 (15.9)	68 (15.8)	0.963	19 (14.5)	25 (19.1)	0.321
CA19-9	>37.0 U/ml	121 (28.1)	124 (61.7)	**<0.001**	66 (50.4)	67 (51.2)	0.902
Surgical procedure	Hepatectomy	64 (32.3)	138 (32.2)	**<0.001**	37 (28.7)	37 (28.7)	0.080
	PD	185 (43.1)	121 (60.6)		79 (60.5)	66 (50.8)	
	GBR	7 (3.5)	75 (17.5)		7 (5.4)	20 (15.4)	
	Simple cholecystectomy	6 (3.0)	31 (7.2)		6 (4.7)	5 (5.4)	
	PVR	11 (5.8)	12 (2.9)	**0.008**	5 (3.9)	6 (4.6)	0.349
	HAR	2 (1.1)	4 (1.0)	**0.037**	2 (1.6)	1 (0.8)	0.302
Operative time	>600 min	58 (30.5)	65 (15.8)	**<0.001**	32 (25.2)	27 (20.8)	0.399
Intraoperative blood loss	>1,000 ml	54 (28.0)	41 (9.9)	**<0.001**	33 (25.6)	21 (16.2)	0.062
Postoperative complications	CD grade ≥1	132 (67.7)	215 (50.5)	**<0.001**	84 (66.1)	86 (50.6)	0.934
Major complications	CD grade ≥3	65 (33.3)	96 (22.5)	**0.004**	40 (31.5)	42 (32.1)	0.922
Postoperative hospital stay	>30 Days	107 (53.2)	128 (29.8)	**<0.001**	69 (52.7)	50 (38.2)	**0.045**
Adjuvant chemotherapy	Yes	67 (33.5)	98 (22.8)	**0.004**	42 (32.3)	46 (35.4)	0.600
Tumor differentiation	Well-differentiated	76 (38.0)	204 (50.0)	**0.006**	57 (43.5)	54 (41.9)	0.788
Lymphatic invasion	Yes	102 (51.0)	134 (31.8)	**<0.001**	63 (48.1)	67 (51.2)	0.875
Vascular invasion	Yes	107 (53.5)	130 (30.8)	**<0.001**	63 (48.1)	62 (47.3)	0.948
Perineural invasion	Yes	136 (68.0)	136 (32.2)	**<0.001**	75 (57.3)	81 (61.8)	0.719
T-Stage*	T3-4	104 (52.0)	129 (30.3)	**<0.001**	59 (45.0)	62 (47.3)	0.576
N-Stage*	N1	71 (35.3)	105 (24.4)	**0.005**	48 (36.6)	51 (38.9)	0.702
Resection status	R0	145 (71.6)	383 (88.7)	**<0.001**	105 (80.1)	105 (80.1)	0.605

AC: Ampullary carcinoma; BMI: body mass index; CA19-9: carbohydrate antigen 19-9; CD: Clavien–Dindo classification; CEA: carcinoembryonic antigen; DCC: distal cholangiocarcinoma; GBC: gallbladder cancer; GBR: gallbladder bed resection; HAR: hepatic artery resection; ICC: intrahepatic cholangiocarcinoma; PD: pancreaticoduodenectomy; PHCC: perihilar cholangiocarcinoma; PVR: portal vein resection. *Union for International Cancer Control TNM staging system (18). Statistically significant *p*-values are shown in bold.

(including pancreaticoduodenectomy) groups, and OS was evaluated by mALBI group within each surgical category. In the hepatectomy-treated group, the median OS was 34 months for the high mALBI group (n=65) and 62 months for the low mALBI group (n=138) (p<0.001). In the non-hepatectomy group, the median OS was 48 months (n=137) and 165 months (n=294), respectively (p<0.001) (Figure 4).

RFS. The difference in RFS between the high and low mALBI groups was significant according to Kaplan–Meier analysis (median=25 *vs*. 131 months; p<0.001) (Figure 2A, lower panel). After PSM, the high mALBI group (n=131) tended to have a worse prognosis in terms of RFS than the low mALBI group (n=131) (median=29 *vs.* 47 months; p=0.063) (Figure 2B, lower panel).

Risk factors for OS in univariate and multivariate analyses. In univariate Cox regression analysis, preoperative CA19-9 level, PVR, differentiation, T-stage, N-stage, lymphatic invasion, vascular invasion, perineural invasion, residual

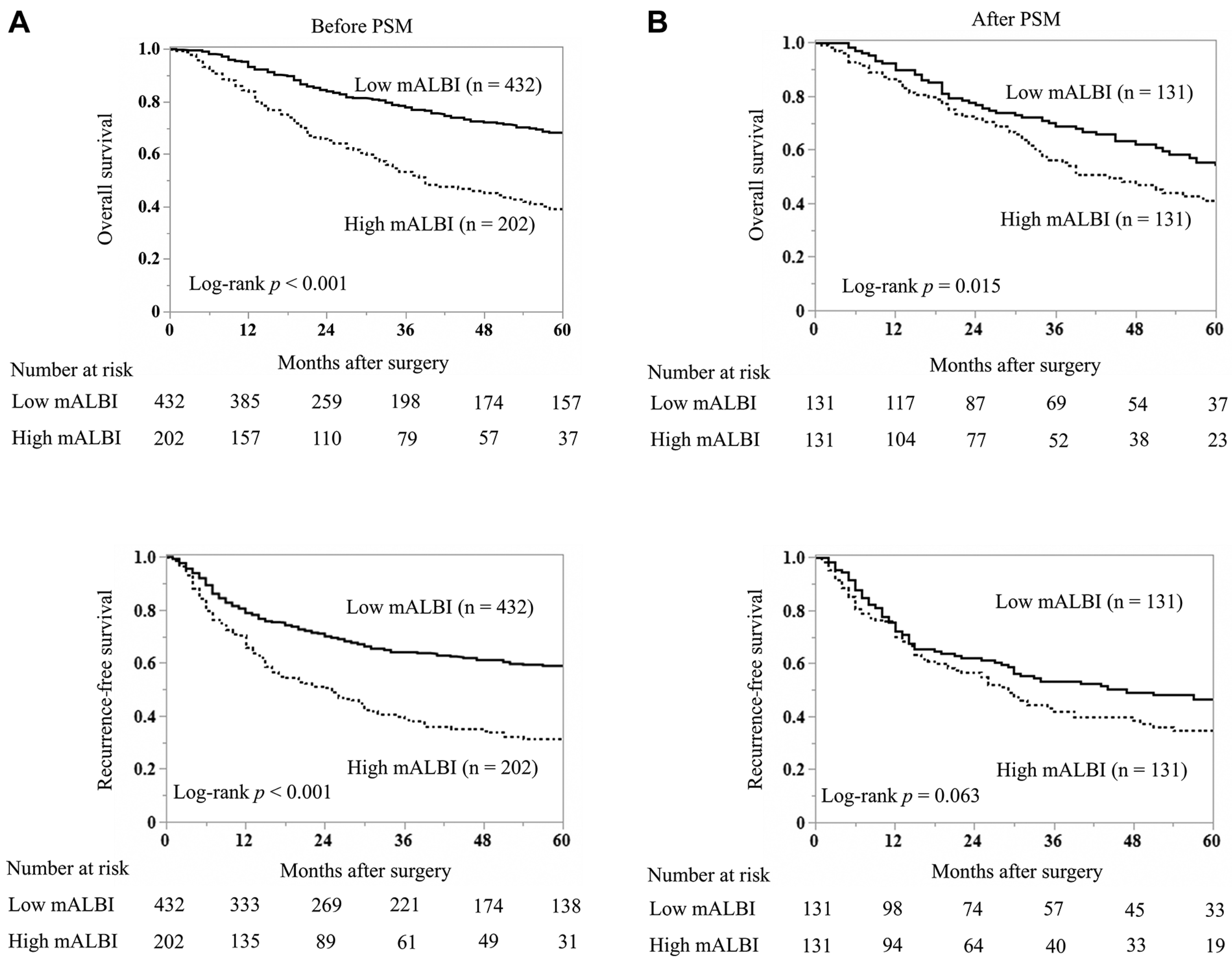


Figure 2. *Kaplan–Meier curves of overall and recurrence-free survival after resection of biliary tract cancer classified by modified albumin–bilirubin (mALBI) group before (A) and after (B) propensity score-matching (PSM).*

cancer, adjuvant chemotherapy, and mALBI were significantly associated with OS (Table II). Variables with a value $p<0.10$ in the univariate analysis along with clinically relevant factors, were included in the multivariate model. Multivariate analysis revealed that high mALBI (HR=1.584, 95% CI=1.077-2.331; $p=0.020$), lymph node metastasis (HR=2.235, 95% CI=1.404-3.557; $p<0.001$), vascular invasion (HR=1.915, 95% CI=1.209-3.032; $p=0.006$), and residual cancer (HR=2.421, 95% CI=1.449-4.044; $p<0.001$) were independent prognostic factors for poor OS (Table II).

Risk factor for RFS in the univariate and multivariate analyses. In univariate Cox regression analysis, preoperative CA19-9 level, differentiation, T-stage, N-stage, lymphatic invasion, vascular invasion, perineural invasion, residual cancer, and adjuvant chemotherapy were significantly associated with RFS (Table III). Although in the univariate Cox regression analysis, high mALBI was not significantly associated with poor RFS ($p=0.067$), it met the threshold for being included in the multivariate analysis; this showed that a high mALBI was an independent prognostic factor for poor RFS (HR=1.447,

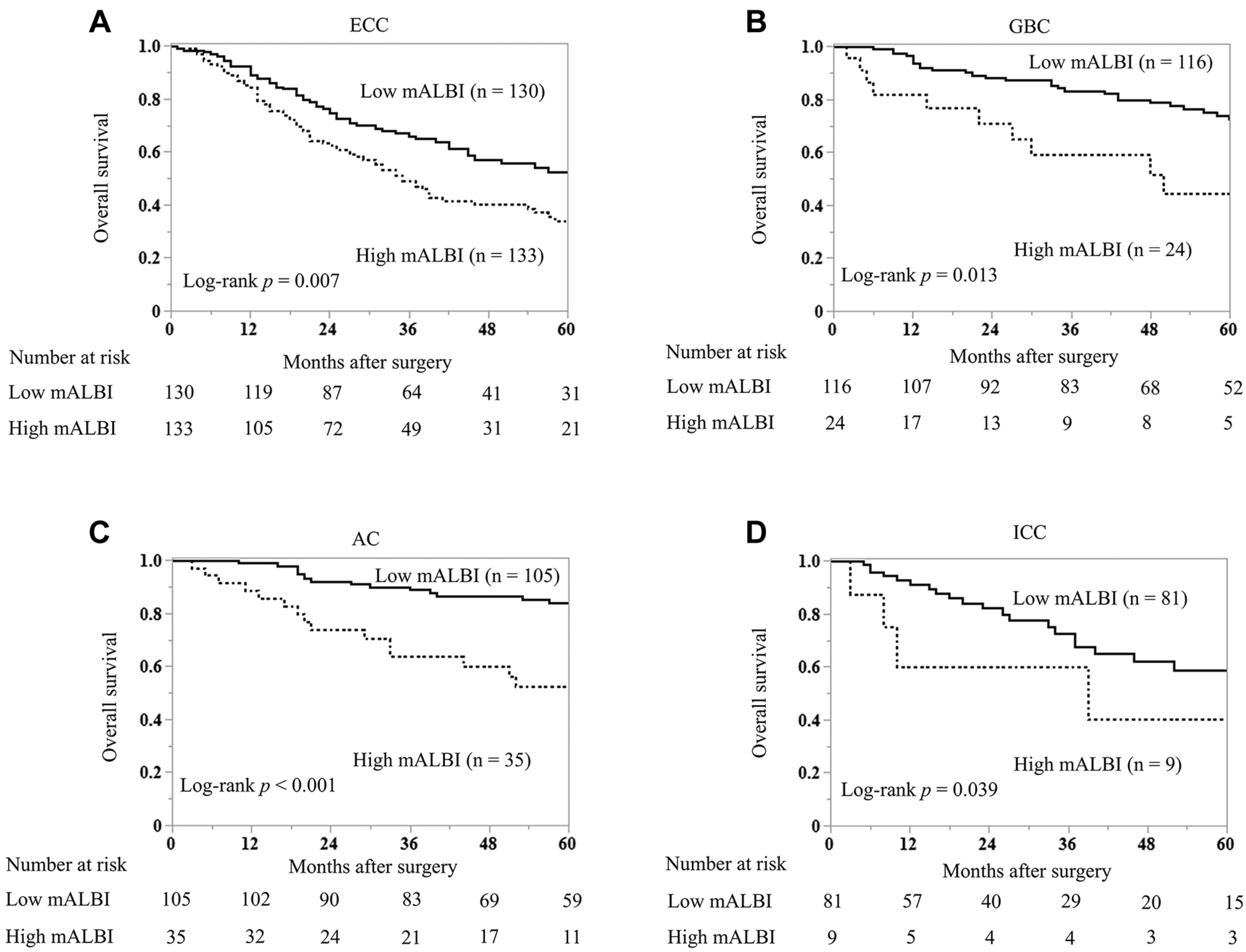


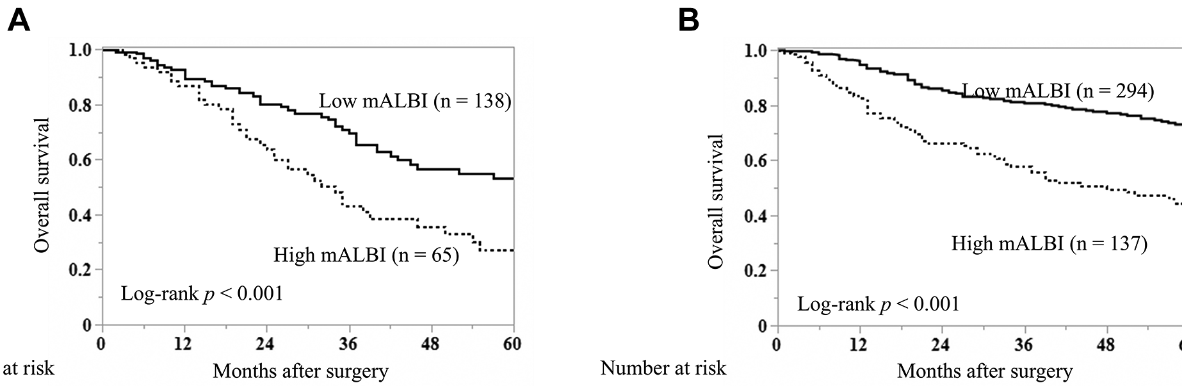
Figure 3. *Kaplan–Meier curves of overall survival of patients after resection of biliary tract cancer classified by subtype and according to modified albumin-bilirubin (mALBI) group. (A) Extrahepatic cholangiocarcinoma (ECC), (B) gallbladder cancer (GBC), (C) ampullary carcinoma (AC), and (D) intrahepatic cholangiocarcinoma (ICC).*

95% CI=1.023-2.046, *p*=0.037) along with the classic factors, lymph node metastasis, vascular invasion and residual cancer.

Discussion

In this multicenter study using PSM, the mALBI grade was demonstrated to be a robust independent prognostic factor in patients who underwent resection for BTC remaining significantly associated with OS after adjustment for established tumor-related variables. These findings highlighted the prognostic value of preoperative hepatic functional reserve in this patient population and indicated that objective functional status has a meaningful impact on long-term outcomes. Accordingly, the mALBI grade might serve as a simple, objective, and clinically applicable tool for preoperative risk stratification in patients with BTC.

The prognostic significance of ALBI score has been consistently demonstrated in various malignancies other than BTC (14-17). In patients with advanced gastric cancer, the ALBI score was demonstrated a valuable



Number at risk						
Low mALBI	138	109	79	56	34	27
High mALBI	65	52	36	18	14	9

Number at risk						
Low mALBI	294	276	229	203	164	130
High mALBI	137	106	77	60	45	29

Figure 4. *Kaplan–Meier curves of overall survival of patients treated with (A) and without (B) hepatectomy according to modified albumin–bilirubin (mALBI) group.*

independent prognostic indicator of postoperative recurrence and disease-specific survival (14). Notably, Ju *et al.* (21) further demonstrated the ALBI score to be an independent prognostic factor even in patients with gastric cancer undergoing curative treatment, supporting its utility beyond advanced disease settings. Similarly, in advanced colon cancer, a high ALBI score was shown to be an independent risk factor for OS and disease-free survival (15). In pancreatic cancer, patients with high ALBI scores and elevated CA19-9 levels exhibited the poorest prognosis, characterized by a significantly reduced 5-year survival rate (16). In the context of BTC, the ALBI score had superior prognostic value compared with the Child–Pugh score in patients with unresectable extrahepatic cholangiocarcinoma, with higher ALBI scores correlating with poorer 1- and 2-year survival rates and an overall worse prognosis (17). More recently, Aydemir *et al.* (22) reported that both ALBI and platelet–ALBI grades are significant prognostic factors in cholangiocellular carcinoma, further reinforcing the importance of liver function-based indices in biliary malignancies. The tumor site subgroup analysis revealed that patients with extrahepatic cholangiocarcinoma, GBC, AC, and ICC in the high mALBI group had a significantly worse prognosis. The mALBI grade was a valuable prognostic factor in all tumor sites of BTC (Figure 3). Moreover, the mALBI grade was a useful prognostic factor not only in the hepatectomy-treated group, but also in the non-hepatectomy group (Figure 4). These results emphasize that the mALBI grade is a valuable prognostic factor in BTC.

The application of PSM in this study allowed for a more rigorous evaluation of mALBI by balancing key baseline characteristics including age, tumor stage, and invasion status. Notably, before matching, the median OS in the low mALBI group was 164 months which is an exceptionally favorable survival for patients with BTC, whereas after matching, the median OS in the low mALBI group was 70 months. This discrepancy possibly suggested baseline imbalances particularly in tumor location, in the pre-matching low mALBI cohort (Table I). After adjustment for tumor location and other prognostic variables by using PSM, the mALBI grade remained an independent prognostic factor. Although PSM was performed to balance baseline characteristics, the covariates included tumor-related factors known to strongly affect prognosis. Therefore, we additionally conducted a multivariate Cox proportional hazards analysis incorporating these tumor-related factors to confirm whether the mALBI grade remained an independent prognostic factor.

The mechanism underlying the association between a high mALBI grade and poor prognosis in patients with BTC remains unclear. Several factors may contribute to this

Table II. *Univariate and multivariate analyses of prognostic factors for overall survival.*

		Univariate			Multivariate		
Variable		HR	95% CI	*p*-Value	HR	95% CI	*p*-Value
mALBI	High *vs.* low	1.554	1.084-2.227	**0.017**	1.584	1.077-2.331	**0.020**
Preoperative cholangitis	Yes *vs.* no	1.289	0.901-1.842	0.165			
CEA	>5.0 *vs.* ≤5.0 ng/ml	1.299	0.811-2.080	0.276			
CA19-9	>37 *vs.* ≤37 U/ml	1.505	1.050-2.157	**0.026**	1.258	0.847-1.868	0.255
PVR	Yes *vs.* no	2.005	0.928-4.332	0.077	1.326	0.542-3.247	0.537
Differentiation	Other *vs.* well-differentiated	1.626	1.121-2.360	**0.011**	1.305	0.851-2.001	0.222
UICC pT*	3,4 *vs.* 1,2	2.304	1.599-3.320	**<0.001**	1.432	0.877-2.340	0.151
Lymph node metastasis	Yes *vs.* no	3.190	2.217-4.591	**<0.001**	2.235	1.404-3.557	**<0.001**
Lymphatic invasion	Yes *vs.* no	2.214	1.498-3.270	**<0.001**	1.126	0.701-1.810	0.623
Vascular invasion	Yes *vs.* no	2.581	1.756-3.794	**<0.001**	1.915	1.209-3.032	**0.006**
Perineural invasion	Yes *vs.* no	2.211	1.446-3.381	**<0.001**	0.733	0.400-1.343	0.315
Residual cancer	Yes *vs.* no	2.377	1.587-3.559	**<0.001**	2.421	1.449-4.044	**<0.001**
Adjuvant chemotherapy	Yes *vs.* no	1.550	1.078-2.229	**0.020**	1.092	0.722-1.652	0.677
Complications (CD grade)	≥3 *vs.* <3	1.242	0.855-1.805	0.254			

CA19-9: Carbohydrate antigen 19-9; CD: Clavien–Dindo classification; CEA: carcinoembryonic antigen; CI: confidence interval; HR: hazard ratio; mALBI: modified albumin-bilirubin score; PVR: portal vein resection. *Union for International Cancer Control TNM staging system (18). Statistically significant *p*-values are shown in bold.

Table III. *Univariate and multivariate analyses of prognostic factors for recurrence-free survival.*

		Univariate			Multivariate		
Variable		HR	95% CI	*p*-Value	HR	95% CI	*p*-Value
mALBI	High *vs.* low	1.352	0.979-1.869	0.067	1.447	1.023-2.046	**0.037**
Preoperative cholangitis	Yes *vs.* no	1.265	0.916-1.746	0.153			
CEA	>5.0 *vs.* ≤5.0 ng/ml	1.500	0.999-2.251	0.051	0.943	0.596-1.491	0.801
CA19-9	>37 *vs.* ≤37 U/ml	1.488	1.076-2.057	**0.016**	1.206	0.848-1.714	0.297
PVR	Yes *vs.* no	1.798	0.875-3.693	0.110			
Differentiation	Other *vs.* well-differentiated	1.676	1.198-2.344	**0.003**	0.746	0.514-1.083	0.297
UICC pT*	3,4 *vs.* 1,2	2.356	1.696-3.274	**<0.001**	1.277	0.837-1.948	0.256
Lymph node metastasis	Yes *vs.* no	2.685	1.940-3.718	**<0.001**	1.800	1.221-2.654	**0.003**
Lymphatic invasion	Yes *vs.* no	2.148	1.514-3.047	**<0.001**	1.144	0.763-1.717	0.515
Vascular invasion	Yes *vs.* no	2.823	1.982-4.021	**<0.001**	1.898	1.265-2.848	**0.002**
Perineural invasion	Yes *vs.* no	2.592	1.741-3.859	**<0.001**	0.981	0.595-1.703	0.981
Residual cancer	Yes *vs.* no	2.470	1.714-3.561	**<0.001**	2.450	1.562-3.843	**<0.001**
Adjuvant chemotherapy	Yes *vs.* no	1.578	1.136-2.191	**0.007**	1.179	0.819-1.698	0.377
Complications (CD grade)	≥3 *vs.* <3	1.158	0.823-1.629	0.401			

CA19-9: Carbohydrate antigen 19-9; CD: Clavien–Dindo classification; CEA: carcinoembryonic antigen; CI: confidence interval; HR: hazard ratio; mALBI: modified albumin-bilirubin score; PVR: portal vein resection. *Union for International Cancer Control TNM staging system (18). Statistically significant *p*-values are shown in bold.

association. A high mALBI grade reflects a reduced serum albumin level and an elevated total bilirubin level; hypoalbuminemia is associated with malnutrition and cachexia and may influence macrophage activation and antitumor immune responses, thereby facilitating tumor progression (23, 24). Hyperbilirubinemia reflects tumor-related biliary obstruction and disease extent in patients with BTC; however, it also represents impaired hepatic functional reserve, chronic inflammation, and impaired physiological reserve. In addition, recent studies have highlighted the importance of host-related factors such as nutritional status and body composition in BTC. Utsumi *et al.* (25) demonstrated that preoperative myosteatosis and prognostic nutritional index are significant predictors of survival in older patients with BTC, while Ikuta *et al.* (26) reported that reduced psoas muscle thickness is associated with poor postoperative outcomes. These findings suggest that mALBI may partly reflect systemic nutritional and metabolic conditions that contribute to oncological outcomes. Therefore, the prognostic value of the mALBI grade in BTC likely reflects a composite effect of both tumor-related factors and host-related conditions. In this study, the mALBI grade stratified prognosis in both the hepatectomy-treated group, in which liver function directly affects surgical strategy, and the non-hepatectomy group, in which liver function is generally considered to have limited influence on the operative procedure (Figure 4). Furthermore, the importance of hepatic functional reserve in surgical oncology is supported by studies in hepatocellular carcinoma, such as that by Kori *et al.* (27), which identified liver function-related factors as key determinants of long-term survival after repeated hepatectomy.

The mALBI score may also influence the feasibility of adjuvant chemotherapy. Miwa *et al*. (28) reported that patients with gastric cancer with a high mALBI score were less likely to continue postoperative adjuvant chemotherapy. Similarly, Kanda *et al.* (14) showed that an elevated mALBI score was associated with difficulty in maintaining adjuvant therapy. However, in the present study, there were no significant differences in the administration of adjuvant chemotherapy between the high and low mALBI groups (32.3% *vs*. 35.4%; Table I). This difference from previous studies of other malignancies is attributable to the lack of effective adjuvant chemotherapy regimens for BTC. Further data collection is required to confirm these findings.

The findings of the present study have important clinical implications. Because mALBI can be easily calculated from routine blood tests, it serves as a simple, objective, and cost-effective preoperative prognostic indicator. Patients with high mALBI scores may require perioperative management interventions such as nutritional intervention, optimization of liver function, and close postoperative monitoring; however, further studies are needed to validate these strategies. The incorporation of mALBI into preoperative risk stratification may help optimize treatment strategies and improve postoperative management of BTC.

Study limitations. Firstly, this was a retrospective multi-center study, and it was not possible to completely exclude selection bias. Although PSM improved comparability between the groups, larger-scale prospective validation studies are needed to confirm these findings. Secondly, although we employed the mALBI classification, a direct comparison with other liver function assessment models, such as the Child–Pugh score or liver stiffness measurements, was not performed and warrants further investigation. Although previous studies, such as that by Wang *et al.* (17), have suggested that the mALBI score may have superior prognostic accuracy compared to the Child–Pugh score in patients with PHCC or DCC, this was not evaluated in the present study. Future studies should explore more comprehensive prognostic models incorporating multiple risk factors. Thirdly, this study did not evaluate dynamic changes in the mALBI score postoperatively or after adjuvant therapy, which may provide additional insights into its prognostic role.

Conclusion

This study demonstrated that mALBI grade is an important prognostic indicator of OS in patients after resection of BTC, even after adjusting for confounding variables through PSM. These findings support incorporating the mALBI score into preoperative risk stratification to optimize treatment strategies and patient management. Further prospective studies are required to validate these results and to explore potential therapeutic interventions for patients with high mALBI scores.

Conflicts of Interest

The Authors declare no conflicts of interest.

Authors' Contributions

TT and HY contributed to the study conception and design. TT performed data analysis and drafted the manuscript. YU contributed to the clinical data collection. MA, DT, MY, YU, TO, KU, HM, IO, SK, and TF critically reviewed and revised the manuscript for important intellectual content. TF provided supervision. TT and HY verified the authenticity of all raw data. All the Authors read and approved the final manuscript and agree to be accountable for all aspects of the work.

Acknowledgements

The Authors would like to thank Editage (www.editage.jp) for English language editing.

Funding

No funding was received.

Artificial Intelligence (AI) Disclosure

During the preparation of this manuscript, a large language model (ChatGPT, OpenAI) was used solely for language editing and stylistic improvements in select paragraphs. No sections involving the generation, analysis, or interpretation of research data were produced by generative AI. All scientific content was created and verified by the authors. Furthermore, no figures or visual data were generated or modified using generative AI or machine-learning-based image enhancement tools.

References

1 Valle JW, Kelley RK, Nervi B, Oh DY, Zhu AX: Biliary tract cancer. Lancet 397(10272): 428-444, 2021. DOI: 10.1016/s0140-6736(21)00153-7

2 Marcano-Bonilla L, Mohamed EA, Mounajjed T, Roberts LR: Biliary tract cancers: epidemiology, molecular pathogenesis and genetic risk associations. Chin Clin Oncol 5(5): 61-61, 2016. DOI: 10.21037/cco.2016.10.09

3 Ouyang G, Liu Q, Wu Y, Liu Z, Lu W, Li S, Pan G, Chen X: The global, regional, and national burden of gallbladder and biliary tract cancer and its attributable risk factors in 195 countries and territories, 1990 to 2017: A systematic analysis for the Global Burden of Disease Study 2017. Cancer 127(13): 2238-2250, 2021. DOI: 10.1002/cncr.33476

4 Ciombor KK, Goff LW: Current therapy and future directions in biliary tract malignancies. Curr Treat Options Oncol 14(3): 337-349, 2013. DOI: 10.1007/s11864-013-0237-5

5 Miyakawa S, Ishihara S, Horiguchi A, Takada T, Miyazaki M, Nagakawa T: Biliary tract cancer treatment: 5,584 results from the Biliary Tract Cancer Statistics Registry from 1998 to 2004 in Japan. J Hepatobil-Pancreat Surg 16(1): 1-7, 2009. DOI: 10.1007/s00534-008-0015-0

6 Seyama Y, Makuuchi M: Current surgical treatment for bile duct cancer. World J Gastroenterol 13(10): 1505-1515, 2007. DOI: 10.3748/wjg.v13.i10.1505

7 Primrose JN, Fox RP, Palmer DH, Malik HZ, Prasad R, Mirza D, Anthony A, Corrie P, Falk S, Finch-Jones M, Wasan H, Ross P, Wall L, Wadsley J, Evans JTR, Stocken D, Praseedom R, Ma YT, Davidson B, Neoptolemos JP, Iveson T, Raftery J, Zhu S, Cunningham D, Garden OJ, Stubbs C, Valle JW, Bridgewater J, BILCAP study group: Capecitabine compared with observation in resected biliary tract cancer (BILCAP): a randomised, controlled, multicentre, phase 3 study. Lancet Oncol 20(5): 663-673, 2019. DOI: 10.1016/s1470-2045(18)30915-x

8 Zhang X, Cai Y, Xiong X, Liu A, Zhou R, You Z, Li F, Cheng N: Comparison of current guidelines and consensus on the management of patients with cholangiocarcinoma: 2022 update. Intractable Rare Dis Res 11(4): 161-172, 2022. DOI: 10.5582/irdr.2022.01109

9 Wiltberger G, Krenzien F, Benzing C, Atanasov G, Klein F, Hau HM, Feldbrügge L, Pratschke J, Schmelzle M, Jonas S: Prognostic accuracy of the seventh edition of the TNM Classification compared with the fifth and sixth edition for distal cholangiocarcinoma. Ann Surg Oncol 23(4): 1320-1326, 2016. DOI: 10.1245/s10434-015-4999-9

10 Johnson PJ, Berhane S, Kagebayashi C, Satomura S, Teng M, Reeves HL, O'Beirne J, Fox R, Skowronska A, Palmer D, Yeo W, Mo F, Lai P, Iñarrairaegui M, Chan SL, Sangro B, Miksad R, Tada T, Kumada T, Toyoda H: Assessment of liver function in patients with hepatocellular carcinoma: a new evidence-based approach—the ALBI grade. J Clin Oncol 33(6): 550-558, 2015. DOI: 10.1200/jco.2014.57.9151

11 Chan AWH, Chong CCN, Mo FKF, Wong J, Yeo W, Johnson PJ, Yu S, Lai PBS, Chan ATC, To KF, Chan SL: Applicability of albumin-bilirubin-based Japan integrated staging score in hepatitis B-associated hepatocellular carcinoma. J Gastroenterol Hepatol 31(10): 1766-1772, 2016. DOI: 10.1111/jgh.13339

12 Wang YY, Zhong JH, Su ZY, Huang JF, Lu SD, Xiang BD, Ma L, Qi LN, Ou BN, Li LQ: Albumin–bilirubin *versus* Child–Pugh score as a predictor of outcome after liver resection for hepatocellular carcinoma. Br J Surg 103(6): 725-734, 2016. DOI: 10.1002/bjs.10095

13 Hiraoka A, Michitaka K, Kumada T, Izumi N, Kadoya M, Kokudo N, Kubo S, Matsuyama Y, Nakashima O, Sakamoto M, Takayama T, Kokudo T, Kashiwabara K, Kudo M: Validation and potential of albumin-bilirubin grade and prognostication in a nationwide survey of 46,681 hepatocellular carcinoma patients in Japan: the need for a more detailed evaluation of hepatic function. Liver Cancer 6(4): 325-336, 2017. DOI: 10.1159/000479984

14 Kanda M, Tanaka C, Kobayashi D, Uda H, Inaoka K, Tanaka Y, Hayashi M, Iwata N, Yamada S, Fujii T, Sugimoto H, Murotani K, Fujiwara M, Kodera Y: Preoperative albumin–bilirubin grade predicts recurrences after radical gastrectomy in patients with pT2-4 gastric cancer. World J Surg 42(3): 773-781, 2018. DOI: 10.1007/s00268-017-4234-x

15 Lee HG, Lim SB, Lee JL, Kim CW, Yoon YS, Park IJ, Kim JC: Preoperative albumin-bilirubin score as a prognostic indicator in patients with stage III colon cancer. Sci Rep 12(1): 14910, 2022. DOI: 10.1038/s41598-022-19329-8

16 Yagyu T, Saito H, Sakamoto T, Uchinaka EI, Morimoto M, Amisaki M, Watanabe J, Tokuyasu N, Honjo S, Ashida K, Fujiwara Y: Preoperative albumin-bilirubin grade as a useful prognostic indicator in patients with pancreatic cancer. Anticancer Res 39(3): 1441-1446, 2019. DOI: 10.21873/anticanres.13260

17 Wang Y, Pang Q, Jin H, Zhou L, Hu X, Qian Z, Man Z, Yang S, Liu H: Albumin-bilirubin grade as a novel predictor of survival in advanced extrahepatic cholangiocarcinoma. Gastroenterol Res Pract 2018: 8902146, 2018. DOI: 10.1155/2018/8902146

18 Edge SB, Compton CC: The American Joint Committee on Cancer: the 7th edition of the AJCC cancer staging manual and the future of TNM. Ann Surg Oncol 17(6): 1471-1474, 2010. DOI: 10.1245/s10434-010-0985-4

19 Kiriyama S, Kozaka K, Takada T, Strasberg SM, Pitt HA, Gabata T, Hata J, Liau KH, Miura F, Horiguchi A, Liu KH, Su CH, Wada K, Jagannath P, Itoi T, Gouma DJ, Mori Y, Mukai S, Giménez ME, Huang WS, Kim MH, Okamoto K, Belli G, Dervenis C, Chan ACW, Lau WY, Endo I, Gomi H, Yoshida M, Mayumi T, Baron TH, de Santibañes E, Teoh AYB, Hwang TL, Ker CG, Chen MF, Han HS, Yoon YS, Choi IS, Yoon DS, Higuchi R, Kitano S, Inomata M, Deziel DJ, Jonas E, Hirata K, Sumiyama Y, Inui K, Yamamoto M: Tokyo Guidelines 2018: diagnostic criteria and severity grading of acute cholangitis (with videos). J Hepatobil-Pancreat Sci 25(1): 17-30, 2018. DOI: 10.1002/jhbp.512

20 Dindo D, Demartines N, Clavien PA: Classification of surgical complications: a new proposal with evaluation in a cohort of 6336 patients and results of a survey. Ann Surg 240(2): 205-213, 2004. DOI: 10.1097/01.sla.0000133083.54934.ae

21 Ju M, Aoyama T, Komori K, Tamagawa H, Tamagawa A, Maezawa Y, Morita J, Onodera A, Endo K, Hashimoto I, Kano K, Hara K, Cho H, Nakazono M, Segami K, Ishiguro T, Onuma S, Oshima T, Yukawa N, Rino Y: The albumin–bilirubin score is a prognostic factor for gastric cancer patients who receive curative treatment. Anticancer Res 42(8): 3929-3935, 2022. DOI: 10.21873/anticanres.15887

22 Aydemir E, Yilmaz F, Türkel A, Ateş Ö, Doğan M: Albumin-bilirubin (ALBI) and platelet-ALBI (PALBI) grades: novel prognostic factors for cholangiocellular carcinoma. In Vivo 39(5): 2976-2985, 2025. DOI: 10.21873/invivo.14098

23 Thurnham DI: Interactions between nutrition and immune function: using inflammation biomarkers to interpret micronutrient status. Proc Nutr Soc 73(1): 1-8, 2014. DOI: 10.1017/s0029665113003662

24 Gupta D, Lis CG: Pretreatment serum albumin as a predictor of cancer survival: a systematic review of the epidemiological literature. Nutr J 9: 69, 2010. DOI: 10.1186/1475-2891-9-69

25 Utsumi M, Inagaki M, Kitada K, Tokunaga N, Yunoki K, Sakurai Y, Okabayashi H, Hamano R, Miyasou H, Tsunemitsu Y, Otsuka S: Preoperative myosteatosis and prognostic nutritional index predict survival in older patients with resected biliary tract cancer. Cancer Diagn Progn 4(2): 147-156, 2024. DOI: 10.21873/cdp.10301

26 Ikuta S, Aihara T, Nakajima T, Kasai M, Yamanaka N: Preoperative psoas muscle thickness to height ratio predicts poor survival after resection of biliary tract cancer. In Vivo 37(2): 879-886, 2023. DOI: 10.21873/invivo.13156

27 Kori M, Shimada K, Hashimoto T: Third liver resection for re-recurrent hepatocellular carcinoma: assessment of the prognostic factors of long-term survival. Cancer Diagn Progn 5(2): 162-170, 2025. DOI: 10.21873/cdp.10426

28 Miwa T, Kanda M, Tanaka C, Kobayashi D, Hayashi M, Yamada S, Nakayama G, Koike M, Kodera Y: Albumin-bilirubin score predicts tolerability to adjuvant S-1 monotherapy after curative gastrectomy. J Gastric Cancer 19(2): 183-192, 2019. DOI: 10.5230/jgc.2019.19.e15