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RESEARCH ARTICLE

An early prognostic marker for determining disease severity in acute cholangitis: CRP/albumin ratio

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Abstract

Introduction: This study was undertaken to investigate the importance of the CRP/albumin ratio (CAR) as an early prognostic marker for determining disease severity in acute cholangitis.

Methods: A total of 366 patients aged >18 years diagnosed with acute cholangitis were included in the study. Acute cholangitis severity was determined according to the 2018 Tokyo criteria.

Results: The study population consisted of 49.2% patients with mild, 24.6% moderate, and 26.2% severe acute cholangitis. The cut-off CAR value for predicting moderate risk compared to the mild risk group was found to be >1 with 73.3% sensitivity and 76.7% specificity (AUC±SE: 0.785±0.03; +PV: 61.1%, -PV: 85.2%; p<0.001). The CAR cut-off value for predicting severe risk compared to the moderate risk group was found to be >2.9 with 71.9% sensitivity and 71.1% specificity (AUC±SE: 0.788±0.03; +PV: 72.6%, -PV: 70.3%; p<0.001). The CAR cut-off value for predicting admission to the intensive care unit (ICU) was >2.5 with 77.4% sensitivity and 74.6% specificity (AUC±SE: 0.803±0.03; +PV: 43.1%, -PV: 90.1%; p<0.001). The CAR cut-off value for predicting mortality was >2.8 with 100% sensitivity and 74.9% specificity (AUC±SE: 0.890±0.03; +PV: 19.5%, -PV: 100%; p<0.001). Compared to its components, the CAR was found to exhibit superior diagnostic performance in predicting moderate or severe risk, ICU admission, and mortality.

Conclusion: We found that the CAR is a good prognostic marker in determining the severity of acute cholangitis in the early period.

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Introduction

Acute cholangitis is an emergency clinical condition with obstruction and infection in the biliary tract resulting in mortality if not treated early.[1] It is necessary to evaluate the clinical condition of the patient, to perform imaging, and to determine the severity of the disease as soon as possible in cases of emergency admission.[2] Early determination of severity allows for immediate biliary system decompression and close clinical follow-up.[3]

The Tokyo 2018 criteria are used to determine severity in cases of acute cholangitis.[4] The Tokyo criteria are applied as part of a multisystemic evaluation with a detailed physical examination and imaging and laboratory findings.[4] For this reason, acute cholangitis cannot be classified as soon as the patient presents and emergency treatment cannot be immediately started. For this reason, early prognostic markers are needed to determine the severity in cases of acute cholangitis.

The C-reactive protein (CRP)/albumin ratio (CAR) is an inflammatory index used to determine the severity of infection and it has recently been frequently used to determine the prognosis of gastrointestinal diseases. In studies of patients with acute pancreatitis and hepatocellular carcinoma, the CAR was found to be an appropriate prognostic marker for clinical outcome.[5-8] Likewise, it was determined that the CAR is successful in predicting disease activity in cases of Crohn's disease.[9] Since acute cholangitis is an inflammatory process occurring in the biliary tract, we hypothesized that the CAR may be a good prognostic marker for this disease as well.

Therefore, this study was planned to investigate whether the CAR can serve as a prognostic marker to determine the severity of cases of acute cholangitis.

Material and Methods

This study was planned retrospectively in Ankara City Hospital's Internal Medicine Clinic, and it was approved by Ankara City Hospital's Ethics Committee (Approval Number E2-22-2195). The study was designed in accordance with good clinical practice guidelines and the 1975 Declaration of Helsinki as updated in 2013. Informed consent was obtained from all participants included in the study.

Patients aged >18 years who applied to the emergency department with symptoms such as abdominal pain, fever, jaundice, or confusion and were diagnosed with acute cholangitis upon further examination were included in the study. Such patients admitted between February 2019 and May 2022 were included in the study in order, regardless of gender. Endoscopic retrograde cholangiopancreatography or percutaneous transhepatic cholangiography was performed in our hospital for all cases included in the study.

Patients with known rheumatic diseases, active infections in any other systems, inflammatory bowel disease, acute pancreatitis, nephrotic syndrome, antibiotic use, metabolic disease, or nutritional disorders were excluded from the study. The clinical demographic findings of the patients, laboratory findings at the time of admission, and imaging findings were accessed via the hospital's electronic information system. The discharge summary files of all patients were examined in detail. Acute cholangitis severity was determined according to the Tokyo Guidelines 2018: Diagnostic Criteria and Severity Grading of Acute Cholecystitis4. CAR values were obtained by dividing the CRP level by direct albumin.

Statistical analysis

Statistical analysis was performed using SPSS 20 for Windows (IBM Corp., Armonk, NY, USA). The normal distribution of data was evaluated by the Shapiro-Wilk test. Numeric variables with and without normal distribution were plotted as mean±standard deviation and median (25th and 75th interquartile range (IQR)), respectively. Categorical variables were given as numeric and percentile values. Chi-square, Yates correction, and Fisher exact tests were used for the comparison of categorical data. The Student t-test or Mann-Whitney U test was used for comparisons of numeric variables between two groups according to the distribution of normality. ANOVA (post hoc: Bonferroni test) or the Kruskal-Wallis H test (post hoc: Dunn test) were used for the comparison of numeric variables between Tokyo severity groups according to the distribution of normality. The relationship between CAR values and numeric variables was determined by Spearman correlation analysis. Logistic regression analysis was used to identify independent predictors of ICU admission. Cox regression analysis was used to identify independent predictors of in-hospital mortality. Evaluation of the diagnostic performance of the CAR was done by receiver operating characteristic curve analysis and cut-off values were determined according to the Youden index method. Values of $p<0.05$ (*) were considered significant in statistical analysis.

Results

The demographic and clinical characteristics of the study population and the distribution of patients according to Tokyo severity are shown in Table 1 in detail. The study population consisted of 366 patients, including 271 cases of choledocholithiasis (74%), 35 cases of benign biliary stenosis (9.6%), 48 cases of malignancy (13.1%), and 12 other causes of cholangitis (3.3%). According to Tokyo severity, 49.2% of the patients had mild, 24.6% had moderate, and 26.2% had severe acute cholangitis. It was determined that the incidence of malignant etiology increased as the Tokyo severity increased. In the severe risk group, the length of stay in the service was longer, the frequency of hospitalization in the ICU was higher, and the duration of hospitalization was longer. It was determined that the mean albumin level decreased as the Tokyo severity increased, while the median CRP and median CAR values increased.

Table 1. Demographic and clinical findings of patients with acute cholangitis

Variables	All population n=366	TOKYO Severity Mild n=180	Moderate n=90	Severe n=96	p
Age, years	65.7±17.2	**57.0±16.2**	74.0±15.4	74.2±12.1	<0.001*
Gender, n(%)					
Female	176(48.1)	87(48.3)	45(50.0)	44(45.8)	0.847
Male	190(51.9)	93(51.7)	45(50.0)	52(54.2)	
Etiology, n(%)					
Benign	318(86.9)	164(91.1)	77(85.6)	77(80.2)	0.035*
Malign	48(13.1)	16(8.9)	13(14.4)	19(19.8)	
Hospitalization, n(%)					
Service	342(93.4)	180(100.0)	84(93.3)	78(81.3)	<0.001*
Length of stay, day	9(6-12)	8(6-10.5)	8.5(6-12)	**10(7-16)**	0.029*
ICU	84(23.0)	3(1.7)	22(24.4)	59(61.5)	<0.001*
Length of stay, day	6(4-10.5)	**8(3-26)**	5(3-9)	6(4-12)	0.235
Composite outcome, n(%)	50(13.7)	5(2.8)	10(11.1)	35(36.5)	<0.001*
Mortality, n(%)	25(6.8)	5(2.8)	4(4.4)	16(16.7)	<0.001*
Duration of hospitalization, day	9(6-14)	8(6-10.5)	9(6-14)	**13(8-17.5)**	<0.001*
White blood count (10^3/μL)	10.1(7.5-12.9)	**9(7-10.8)**	12.6(9.7-15.8)	11.6(8.2-15.2)	<0.001*
Platelet (10^3/μL)	239(189-308)	**276(216.5-330.5)**	**234(193-287)**	**162.5(106-234.5)**	<0.001*
Hemoglobin (g/dL)	13.3±2.0	**13.7±1.9**	**13.1±1.8**	**12.5±2.2**	<0.001*
Hematocrit (%)	40.2±5.8	**41.5±5.3**	39.2±5.3	38.6±6.5	<0.001*
UREA (mg/dl)	38(25-53)	**28.5(21-38)**	**40(29-51)**	**64.5(47-88)**	<0.001*
Sodium (mEq/L)	137.7±3.6	138.5±3.1	137.8±3.8	**136.3±4.2**	<0.001*
Potassium (mEq/L)	4.1±0.5	4.1±0.4	4.1±0.5	4.0±0.6	0.606
Calcium (mEq/L)	8.9±0.7	**9.2±0.5**	**8.8±0.7**	**8.4±0.7**	<0.001*
ALT (U/L)	207.5(107-348)	248(133.5-398.5)	184(115-337)	**133(70.5-242.5)**	<0.001*
AST (U/L)	182.5(98-314)	189(103-329.5)	205(112-330)	141.5(82-259.5)	0.061
ALP (U/L)	256.5(185-423)	243.5(175-396.5)	291.5(199-447)	273(195.5-371.5)	0.136
GGT (U/L)	435.5(248-674)	497(264.5-736)	477(295-740)	**333(180-530.5)**	<0.001*
Total bilirubin (mg/dl)	4.7(2.9-7.6)	**3.6(2.3-6.1)**	5.9(3.8-8.7)	5.6(4-9.5)	<0.001*
Direct bilirubin (mg/dl)	3.2(1.9-5.3)	**2.3(1.3-4.2)**	4.1(2.5-5.8)	4.1(2.8-6.8)	<0.001*
Albumin (g/dl)	39.4±5.7	**42.3±4.2**	**38.7±5.2**	**34.7±5.2**	<0.001*
CRP (mg/L)	45(20-95)	**24(13-41.5)**	**63(40-99)**	**117(62.5-180.5)**	<0.001*
Procalcitonin (μg/L)	0.5(0.2-5.9)	**0.2(0.1-0.5)**	**1.1(0.3-7.4)**	**5.5(1.1-36)**	<0.001*

Data are mean±standard deviation or median (IQR), or number (%). *p<0.05 indicates statistical significance. Bold characters show the difference between groups. Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; CAR, CRP to albumin ratio; CRP, C reactive protein; GGT, gamma glutamyl transferase; ICU, intensive care unit; INR, international normalized ratio

The mean age, malignancy etiology, severe risk ratio, and mortality rate were higher among patients admitted to the ICU compared to non-admitted patients. Median CAR values were found to be higher among patients admitted to the ICU compared to those who were not admitted (3.4 vs. 1.3; p<0.001) (Table2). The in-hospital mortality rate was 6.8% (n:25).

Table 2. Factors associated with hospitalization of the intensive care unit in patients with acute cholangitis

Variables	ICU admission No n=282	Yes n=84	p
Age, years	62.5±17.5	76.3±10.8	<0.001*
Gender, n(%)			
Female	136(48.2)	40(47.6)	0.922
Male	146(51.8)	44(52.4)	
Etiology, n(%)			
Benign	254(90.1)	64(76.2)	0.001*
Malign	28(9.9)	20(23.8)	
TOKYO severity, n(%)			
Mild	177(62.8)	3(3.6)	
Moderate	68(24.1)	22(26.2)	<0.001*
Severe	37(13.1)	59(70.2)	
Hospitalization of service, n(%)	282(100.0)	60(71.4)	<0.001*
Length of stay, day	8(6-11)	11(6.5-16.5)	0.075
Composite outcome, n(%)	4(1.4)	46(54.8)	<0.001*
Mortality, n(%)	4(1.4)	21(25.0)	<0.001*
Duration of hospitalization, day	8(6-11)	14(9-19.5)	<0.001*
White blood count (10^3/μL)	9.7(7.2-12.3)	12(9-15.4)	<0.001*
Platelet (10^3/μL)	249(199-312)	206.5(135-291.5)	0.001*
Hemoglobin (g/dL)	13.4±2.0	12.8±1.9	0.029*
Hematocrit (%)	40.4±5.8	39.2±5.8	0.077
UREA (mg/dL)	32(23-47)	55.5(41.5-81)	<0.001*
Sodium (mEq/L)	137.9±3.5	137.1±4.1	0.076
Potassium (mEq/L)	4.1±0.5	4.1±0.6	0.520
Calcium (mEq/L)	9.0±0.7	8.5±0.7	<0.001*
ALT (U/L)	224(115-371)	162.5(82-262)	0.005*
AST (U/L)	184.5(103-317)	176.5(92.5-308)	0.619
ALP (U/L)	247(179-403)	311.5(200-441)	0.093
GGT (U/L)	445(251-708)	375(237-565.5)	0.097
Total bilirubin (mg/dl)	4.3(2.7-7.1)	6(4.3-9.4)	<0.001*
Direct bilirubin (mg/dl)	2.9(1.7-4.8)	4.5(3-6.8)	<0.001*
Albumin (g/dl)	40.6±5.3	35.6±5.3	<0.001*
CRP (mg/L)	37(17-71)	105.5(52-179)	<0.001*
Procalcitonin (μg/L)	0.3(0.1-3.9)	3.1(0.6-19.7)	<0.001*
INR	1.2±0.4	1.4±0.4	<0.001*
CAR	0.9(0.4-1.8)	3.2(1.5-5.0)	<0.001*

Data are mean±standard deviation or median (IQR), or number (%). *p<0.05 indicates statistical significance. Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; CAR, CRP to albumin ratio; CRP, C reactive protein; GGT, gamma glutamyl transferase; ICU, intensive care unit; INR, international normalized ratio

No significant correlation was found between Tokyo severity and mortality, but ICU hospitalization was associated with an increased risk of mortality (HR: 7.14; p<0.001). Decreases in hemoglobin, hematocrit, sodium, calcium, and albumin levels were found to be associated with an increased risk of mortality. Increases in urea, CRP, and CAR values were associated with an increased risk of mortality (Table 3).

Table 3. Factors associated with in-hospital mortality in patients with acute cholangitis

Variables	Survival		Univariable Regression			
	Alive n=341	Exitus n=25	HR	95% CI lower	95% CI upper	p
Age, years	65.0±17.3	74.8±13.8	1.02	0.99	1.05	0.216
Gender, n(%)						
Female	168(49.3)	8(32.0)	ref			
Male	173(50.7)	17(68.0)	1.14	0.47	2.78	0.773
Etiology, n(%)						
Benign	254(90.1)	64(76.2)	ref			
Malign	28(9.9)	20(23.8)	6.68	2.76	16.15	<0.001*
TOKYO severity, n(%)						
Mild	175(51.3)	5(20.0)	ref			
Moderate	86(25.2)	4(16.0)	1.01	0.27	3.81	0.993
Severe	80(23.5)	16(64.0)	2.28	0.79	6.62	0.129
Hospitalization, n(%)						
Service	326(95.6)	16(64.0)	0.05	0.02	0.13	<0.001*
Length of stay, day	8(6-12)	16(10.5-23)	0.88	0.81	0.96	0.003
ICU	63(18.5)	21(84.0)	7.14	2.32	21.96	<0.001*
Length of stay, day	6(4-10)	6(3-14)	0.97	0.92	1.02	0.215
Composite outcome, n(%)	25(7.3)	25(100.0)	29.30	2.09	169.20	0.006*
Duration of hospitalization, day	9(6-13)	14(7-29)			-	
White blood count (10^3/μL)	10(7.5-12.8)	11.8(8.7-15.3)	1.02	0.97	1.08	0.468
Platelet (10^3/μL)	240(193-307)	217(158-355)	1.00	1.00	1.01	0.115
Hemoglobin (g/dL)	13.4±2.0	11.5±2.0	0.72	0.60	0.87	<0.001*
Hematocrit (%)	40.5±5.6	35.3±6.0	0.90	0.84	0.96	<0.001*
UREA (mg/dl)	36(25-51)	58(40-87)	1.02	1.01	1.03	<0.001*
Sodium (mEq/L)	138.0±3.5	134.6±3.9	0.81	0.73	0.90	<0.001*
Potassium (mEq/L)	4.1±0.5	4.2±0.8	1.30	0.63	2.65	0.479
Calcium (mEq/L)	8.9±0.7	8.2±0.7	0.40	0.23	0.71	0.002*
ALT (U/L)	224(121-358)	76(38-121)	0.99	0.99	1.00	0.004*
AST (U/L)	188(103-319)	98(66-218)	1.00	0.99	1.00	0.161
ALP (U/L)	250(184-389)	423(304-631)	1.00	1.00	1.00	0.816
GGT (U/L)	439(251-691)	327(169-574)	1.00	1.00	1.00	0.441
Total bilirubin (mg/dl)	4.6(2.9-7.3)	9.1(4.5-11.7)	1.02	0.97	1.07	0.492
Direct bilirubin (mg/dl)	3.2(1.9-5.1)	6.8(3.6-9.2)	1.03	0.96	1.10	0.389
Albumin (g/dl)	40.1±5.1	30.8±5.7	0.83	0.77	0.88	<0.001*
CRP (mg/L)	42(19-83)	112(79-161)	1.01	1.00	1.01	0.021*
Procalcitonin (μg/L)	0.5(0.1-5.5)	1.4(0.7-13)	1.00	0.98	1.01	0.747
INR	1.2±0.4	1.5±0.5	0.97	0.51	1.85	0.937
CAR	1.1(0.5-2.2)	3.8(2.8-5.2)	1.35	1.14	1.59	<0.001*

*p<0.05 indicates statistical significance. Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; CAR, CRP to albumin ratio; CRP, C reactive protein; GGT, gamma glutamyl transferase; ICU, intensive care unit; INR, international normalized ratio

Positive correlations were observed between CAR values and age (r=0.466; p<0.001), length of hospital stay (r=0.238; p<0.001), white blood cell (WBC) count (r=0.326; p<0.001), and procalcitonin (r=0.657; p<0.001). The relationships between CAR values and laboratory findings are shown in Table 4.

Table 4. Factors associated with CAR levels in patients with acute cholangitis

Variables	CAR	
	r	p
Age	0.466	<0.001*
Length of stay in service	0.127	0.019*
Length of stay in ICU	0.088	0.427
Duration of hospitalization	0.238	<0.001*
White blood count	0.326	<0.001*
Platelet	-0.377	<0.001*
Hemoglobin	-0.237	<0.001*
Hematocrit	-0.244	<0.001*
UREA	0.551	<0.001*
Sodium	-0.314	<0.001*
Potassium	-0.051	0.329
Calcium	-0.468	<0.001*
ALT	-0.295	<0.001*
AST	-0.207	<0.001*
ALP	0.096	0.066
GGT	-0.099	0.057
Total bilirubin	0.239	<0.001*
Direct bilirubin	0.267	<0.001*
Procalcitonin	0.657	<0.001*
INR	0.553	<0.001*

*p<0.05 indicates statistical significance. Abbreviations: ALT, alanine aminotransferase; AST, aspartate aminotransferase; ALP, alkaline phosphatase; CAR, CRP to albumin ratio; CRP, C reactive protein; GGT, gamma glutamyl transferase; ICU, intensive care unit; INR, international normalized ratio

In the multivariate regression model, in which the variables associated with Tokyo severity were included, the independent predictors of moderate risk compared to mild risk were found to be older age, higher WBC count, and higher total bilirubin and CAR values. Independent predictors of severe risk compared to moderate risk were increased procalcitonin, urea, and CAR values. According to this model, compared to the group with mild risk, a 1-unit increase in the CAR increased the likelihood of moderate risk by 1.75 times (OR: 1.75; p=0.003), while compared to moderate risk, it increased the likelihood of severe risk by 1.63 times (OR: 1.63; p<0.001) (Table 5).

Table 5. Independent predictors for endpoints

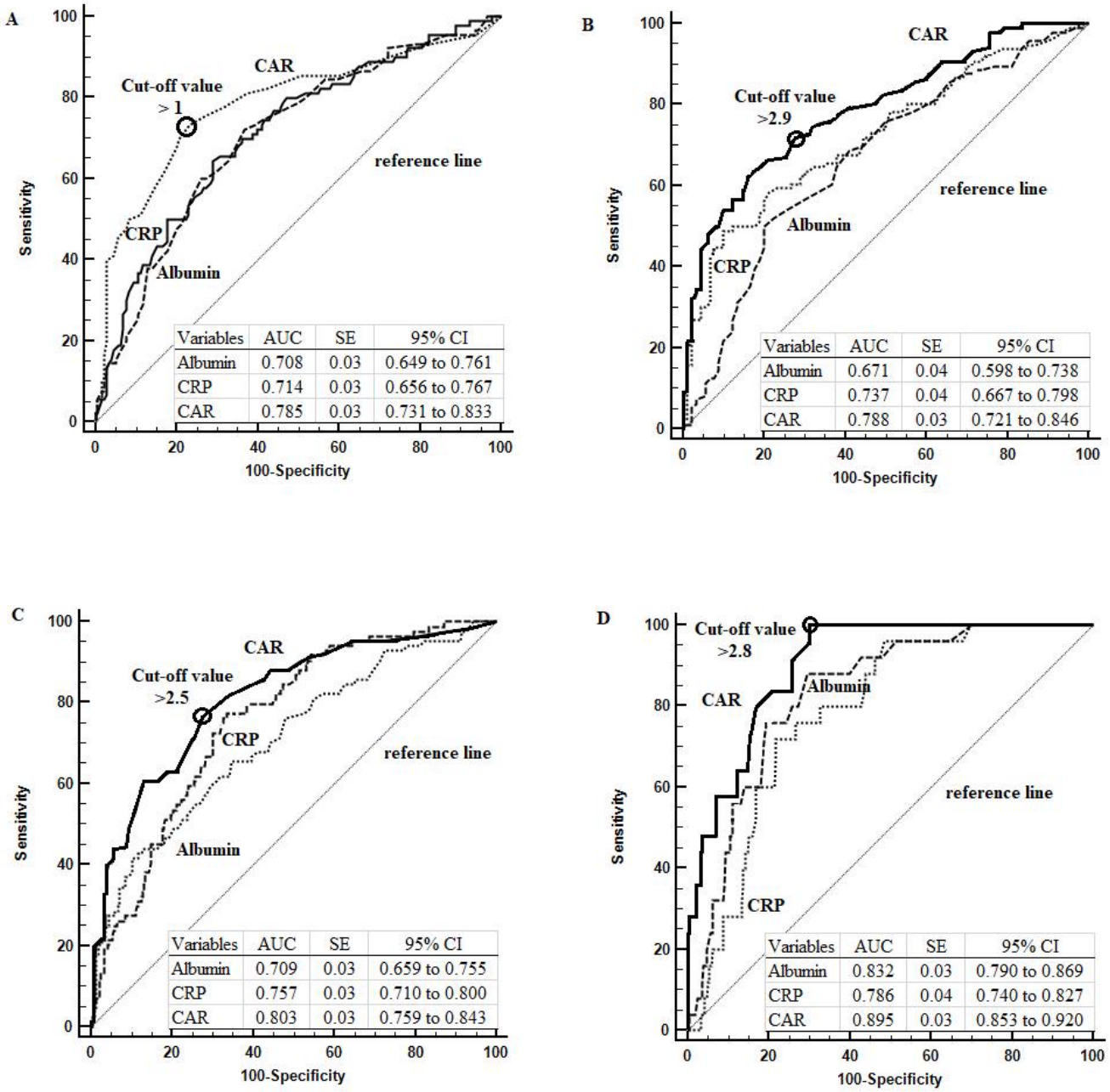
Variables	OR	95% CI Lower	95% CI Upper	p
TOKYO Severity				
Moderate (ref: mild)				
Age	1.06	1.03	1.09	<0.001*
White blood count	1.23	1.12	1.35	<0.001*
Total bilirubin	1.15	1.06	1.24	0.001*
CAR	1.75	1.21	2.53	0.003*
		Nagelkerke R^2= 0.537, p< 0.001		
Severe (ref: moderate)				
Procalcitonin	1.04	1.02	1.08	0.004*
UREA	1.03	1.01	1.04	0.001*
CAR	1.63	1.27	2.08	<0.001*
		Nagelkerke R^2= 0.493, p< 0.001		
ICU admission				
Age	1.04	1.01	1.07	0.006*
Tokyo Severity				
Mild	ref			
Moderate	9.09	2.45	33.78	0.001*
Severe	30.67	8.18	115.02	<0.001*
Procalcitonin	1.02	1.01	10.3	0.035
CAR	1.27	1.06	1.53	0.011*
		Nagelkerke R^2= 0.543, p< 0.001		
Mortality	HR			
ICU admission	3.47	1.08	9.71	0.028*
UREA	1.02	1.01	1.03	0.037
CAR	1.36	1.14	1.63	0.001*
		-2Log Likelihood=168.6. p<0.001		

*p<0.05 indicates statistical significance.
Abbreviations: CI, confidence interval; CAR, CRP to albumin ratio; HR, hazard ratio; ICU, intensive care unit; OR, odds ratio;

Older age, increased Tokyo severity, and increased procalcitonin and CAR values were determined as independent predictors of ICU admission. Accordingly, it was determined that a 1-unit increase in the CAR increased the risk of admission to the intensive care unit by 1.27 times (OR: 1.27; p=0.011). ICU admission, increased urea, and increased CAR were independent predictors of mortality. It was determined that a 1-unit increase in the CAR increased the risk of mortality by 1.36 times (OR: 1.36; p=0.001).

The cut-off value of the CAR in predicting moderate risk compared to mild risk was found to be >1 with 73.3% sensitivity and 76.7% specificity (AUC±SE: 0.785±0.03; +PV: 61.1%, -PV: 85.2%; p<0.001) (Figure 1A). The cut-off value of the CAR in predicting severe risk compared to moderate risk was found to be >2.9 with 71.9% sensitivity and 71.1% specificity (AUC±SE: 0.788±0.03; +PV: 72.6%, -PV: 70.3%; p<0.001) (Figure 1B). The cut-off value of the CAR in predicting admission to the ICU was >2.5 with 77.4% sensitivity and 74.6% specificity (AUC±SE: 0.803±0.03; +PV: 43.1%, -PV: 90.1%; p<0.001) (Figure 1C). The cut-off value of the CAR in predicting mortality was >2.8 with 100% sensitivity and 74.9% specificity (AUC±SE: 0.890±0.03; +PV: 19.5%, -PV: 100%; p<0.001) (Figure 1D). Compared to its components, the CAR was found to exhibit superior diagnostic performance in predicting moderate or severe risk, ICU admission, and mortality (Figure 1).

Figure 1. Diagnostic performance assessment of CAR values in predicting moderate (A) and severe (B) Tokyo severity, ICU admission (C), and in-hospital mortality (D)



Discussion

In the present study, we investigated whether the CAR could predict severity as an early prognostic marker in acute cholangitis. To our knowledge, this study is the first of its kind in this field. We determined that the CAR, which can be calculated shortly after admission to the emergency department, successfully predicts severity among patients with acute cholangitis. It also proved to be a good prognostic marker for the prediction of ICU admission and mortality.

Determining the severity of acute cholangitis is very important in making decisions about the type of patient follow-up, prognosis, treatment strategies, and the timing of biliary decompression.[10] The 2018 Tokyo criteria provide convenience to the clinician in the management of acute cholangitis. According to the guidelines, in the event of failure of any organ (kidneys, lungs, heart, liver, hematological system, etc.), the patient is considered to have severe acute cholangitis, while moderate acute cholangitis is considered in the presence of deterioration in clinical and laboratory parameters. Mild acute cholangitis is diagnosed for patients who are not classified as having moderate or severe cases.[4]

We could not find any previous study examining the prognostic significance of the CAR in acute cholangitis. In a study conducted with acute pancreatitis patients, however, it was determined that the CAR was a prognostic marker associated with mortality.[6] In a study conducted with patients with Crohn's disease, it was determined that CAR values were associated with the Crohn's disease activity index.[9] In a study of ulcerative colitis, it was determined that the CAR was closely related to clinical disease severity.[11] The CAR was also found to be closely related to prognosis in cases of esophagus, stomach, colorectal, and liver malignancies and cholangiocarcinoma.[7,12-15]

In the literature, there are studies on procalcitonin, an inflammatory marker similar to the CAR, and acute cholangitis. In these studies, it was concluded that the level of procalcitonin increases in acute cholangitis and may be an early prognostic marker in determining the severity of acute cholangitis.[16-19] Similarly, in a study conducted on presepsin, an inflammatory marker, it was concluded that presepsin is a good marker for determining the severity of acute cholangitis.[20]

In our study, CAR values were found to differ among mild, moderate, and severe stages of acute cholangitis. Along with those results, relationships were found between many parameters of the 2018 Tokyo, Sepsis-Related Organ Failure Assessment (SOFA), and Systemic Inflammatory Response Syndrome (SIRS) criteria and CAR values. For example, positive correlations were found between CAR values and age, WBC count, urea, total bilirubin, direct bilirubin, indirect bilirubin, procalcitonin, and international normalized ratio values, and negative correlations were found for platelet count, hemoglobin, and hematocrit. These results show that the CAR is a marker that works similarly to the 2018 Tokyo, SOFA, and SIRS criteria.

Many studies have shown that procalcitonin is a good marker in the classification of acute cholangitis.[14-17] In our study, while procalcitonin did not predict moderate acute cholangitis in regression analysis, it predicted severe acute cholangitis with an OR lower than that of the CAR. Since procalcitonin is not a molecule that can be studied directly in all centers, it is a less useful predictor than the CAR.

In our study, it was determined that the CAR, with different cut-off values, classified acute cholangitis in accordance with the 2018 Tokyo guidelines. In regression analysis, the CAR and the 2018 Tokyo criteria were determined as parameters that could predict admission to the ICU. While the CAR performed well in predicting mortality, the Tokyo criteria were not associated with mortality. Based on these results, we can say that the CAR, which is a marker that can be calculated shortly after a patient's entry to the emergency room, can be used to classify acute cholangitis similarly to the 2018 Tokyo criteria and to predict admission to the ICU, but it is superior to the Tokyo criteria in that it can also predict mortality.

The main limitation of our study is its retrospective nature. However, the systematic recording of patients' clinical and demographic data, physical examination findings, laboratory findings, and imaging results minimized that limitation. Another limitation is that it was not known when acute cholangitis began in these cases or how long after the onset of this clinical condition the patients presented. Another limitation is that we do not know how CAR values changed during the course of acute cholangitis, i.e., from hospitalization to the clinical outcome.

Conclusion

In this study, we found that the CAR is a good prognostic marker for the detection of severe acute cholangitis in the early period. We concluded that the CAR is superior to other prognostic mar-

kers in that it predicts early admission to the ICU and mortality in cases of acute cholangitis. Since the CAR can be easily calculated, obtained quickly, and is a cheap and practical method, it provides great convenience for the clinician to determine the severity of acute cholangitis at the time of the patient's first application. We think that it would be valuable to continue studying the diagnostic performance of this marker in prospective studies to support the wider use of the CAR in clinical practice.

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