Article

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Predictive Value of CRP/Albumin Ratio For Treatment Response to PTGBD in Patients With High-Risk Acute Cholecystitis

Chuncui Ye[1,†], Anqing Luo[2,†], Jun Wang[1,*]

[1]Department of Gastroenterology, The Affiliated Hospital of Xuzhou Medical University, 221002 Xuzhou, Jiangsu, China
[2]Department of General Surgery, Lianshui People's Hospital of Kangda College Affiliated to Nanjing Medical University, 223400 Huai'an, Jiangsu, China
*Correspondence: jsxzwj123321@163.com (Jun Wang)
[†]These authors contributed equally.
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Background: Patients with high-risk acute cholecystitis are challenging to manage because many cannot tolerate early surgery. Percutaneous transhepatic gallbladder drainage (PTGBD) is therefore commonly used; however, the clinical response after drainage is not always satisfactory. Reliable indicators for early identification of patients at risk of poor treatment response remain limited. Although inflammatory and nutritional biomarkers have shown potential value in risk stratification, their role in predicting response to PTGBD has not been fully clarified. Accordingly, this study aims to evaluate the predictive value of the preoperative C-reactive protein/albumin ratio (CAR) for poor treatment response in high-risk patients with acute cholecystitis undergoing PTGBD.

Methods: Clinical data from 309 patients with high-risk acute cholecystitis who underwent PTGBD at our institution between January 2023 and January 2025 were retrospectively reviewed. Based on post-procedural treatment response, patients were categorized into a good response group (n = 231) and a poor response group (n = 78). Receiver operating characteristic (ROC) curve analysis was applied to assess the predictive performance of CAR. Multivariable logistic regression analysis was used to determine independent predictors of poor treatment response, and a predictive model was subsequently developed.

Results: Seventy-eight patients (25.2%) developed poor treatment response. Preoperative CAR was higher in the poor response group than in the good response group [5.82 (3.65–8.96) vs 2.68 (1.35–4.52), $p < 0.001$]. ROC curve analysis showed that the area under the curve (AUC) of CAR for predicting poor treatment response was 0.812 (95% confidence interval (CI): 0.758–0.866), which was higher than that of C-reactive protein (CRP) (AUC = 0.756) and albumin (AUC = 0.718) ($p < 0.05$); the optimal cutoff value was 3.85, with a sensitivity of 74.4% and specificity of 76.2%. Multivariable logistic regression analysis showed that CAR $\geq$3.85 (odds ratio (OR) = 3.42, 95% CI: 1.89–6.18), TG18 Grade III (OR = 2.28, 95% CI: 1.26–4.12), time from onset to PTGBD $\geq$72 h (OR = 2.15, 95% CI: 1.18–3.92), diabetes mellitus (OR = 1.86, 95% CI: 1.04–3.33), and CCI $\geq$4 (OR = 1.92, 95% CI: 1.08–3.41) were independent risk factors for poor treatment response (all $p < 0.05$). The high CAR group (CAR $\geq$3.85) had longer time to temperature normalization, abdominal pain relief, and WBC normalization compared to the low CAR group (all $p < 0.001$).

Conclusion: Preoperative CAR shows good performance in identifying high-risk acute cholecystitis patients who are more likely to experience an unfavorable response to PTGBD. A CAR value $\geq$3.85 is associated with an increased likelihood of poor treatment response and may assist clinicians in early risk stratification and treatment planning.

Keywords: acute cholecystitis; percutaneous transhepatic gallbladder drainage; C-reactive protein/albumin ratio; prediction; treatment response

Introduction

Acute cholecystitis is a common acute abdominal condition in clinical practice, and remains an important healthcare burden, particularly among older patients and those with substantial comorbidities [1]. Clinically, acute cholecystitis is classified into three grades of severity: mild, moderate, and severe. Moderate to severe patients often present with organ dysfunction or severe local inflammation, significantly increasing surgical risk [2]. For patients with severe systemic disease or substantial comorbidity burden, early cholecystectomy may be associated with a higher risk of perioperative complications, although short-term mortality does not appear to be significantly increased [3]. Percutaneous transhepatic gallbladder drainage (PTGBD), as a minimally invasive interventional approach, can effectively reduce intracystic pressure and control infec-

tion. It is now widely recommended as the first-line biliary drainage method for patients with high-risk acute cholecystitis [4]. However, in clinical practice, some patients experience slow resolution of inflammation after PTGBD, with unsatisfactory symptom improvement, and some even require emergency surgical intervention [5]. Currently, studies investigating predictors of poor treatment response to PTGBD are limited, and simple, reliable early warning indicators remain lacking.

C-reactive protein (CRP) is widely used as an indicator of systemic inflammatory activity, whereas serum albumin reflects not only nutritional status but also host immune competence [6]. In recent years, the CRP/albumin ratio (CAR) has been proposed as an integrated biomarker capturing both inflammatory response and nutritional–immune condition, and has shown promising prognostic utility in patients with sepsis and other severe infections [7]. Compared with single inflammatory parameters, CAR appears to better represent the overall inflammatory burden and has been reported to correlate closely with disease severity and unfavorable clinical outcomes in infectious settings [8]. Nevertheless, evidence regarding the role of CAR in acute cholecystitis remains limited [9]. Therefore, the present study evaluated the predictive performance of preoperative CAR for poor treatment response to PTGBD in high-risk patients with acute cholecystitis, with the aim of facilitating early risk stratification and informing clinical decision-making.

Methods

Study Design and Subjects

This was a single-center retrospective cohort study. Clinical data were collected from patients with acute cholecystitis who underwent percutaneous transhepatic gallbladder drainage (PTGBD) at The Affiliated Hospital of Xuzhou Medical University between January 2023 and January 2025. The study was approved by the Medical Ethics Committee of The Affiliated Hospital of Xuzhou Medical University (Approval No. XYFY2025-K1437-03). Given the retrospective nature of the study and the use of anonymized clinical data, the requirement for informed consent was waived by the ethics committee. All procedures involving human participants were conducted in accordance with the Declaration of Helsinki.

Inclusion and Exclusion Criteria

Inclusion criteria: (1) Age $\geq$18 years; (2) Diagnosed with acute cholecystitis according to the Tokyo Guidelines 2018 (TG18) diagnostic criteria; (3) Diagnosed with moderate (Grade II) or severe (Grade III) acute cholecystitis according to TG18 severity grading criteria, or with high surgical risk factors (ASA classification $\geq$III, Charlson Comorbidity Index [CCI] $\geq$3); (4) Underwent PTGBD treatment due to high risk of emergency surgery or poor general condition; (5) Completed serum CRP and albumin testing within 24 hours before PTGBD.

Exclusion criteria: (1) Combined with choledocholithiasis, acute cholangitis, or acute pancreatitis; (2) Gallbladder malignancy or suspected malignant lesion; (3) Other biliary drainage procedures performed before PTGBD; (4) Combined with acute infectious diseases at other sites; (5) Use of immunosuppressants or glucocorticoids within 2 weeks before admission; (6) Combined with autoimmune diseases, hematological diseases, or end-stage liver disease (Child-Pugh class C); (7) Pregnant or lactating women; (8) Incomplete clinical data, defined as missing key data required for outcome determination (including any one of temperature, pain score, or complete blood count results within 72 hours after PTGBD).

According to the above criteria, 309 patients were finally included for analysis.

PTGBD Procedure

PTGBD was performed by three senior interventional radiologists, each with over 5 years of experience. All procedures were conducted under real-time ultrasound guidance using a LOGIQ E9 ultrasound system (GE Healthcare, Chicago, IL, USA). After routine skin preparation and sterile draping, patients were positioned supine and received local anesthesia with 2% lidocaine hydrochloride injection (Hualu Pharmaceutical Co., Ltd., Liaocheng, China). Coagulation status was assessed before drainage, and the procedure was undertaken only when the platelet count was $\geq 50 \times 10^9$/L and the international normalized ratio (INR) was $\leq$1.5; abnormalities were corrected when necessary. Prophylactic intravenous antibiotics, including ceftriaxone 2 g ceftriaxone sodium for injection (Shandong Luoxin Pharmaceutical Group Co., Ltd., Linyi, China) or levofloxacin 0.5 g levofloxacin hydrochloride injection (Yangtze River Pharmaceutical Group Co., Ltd., Taizhou, China), were administered 30 minutes prior to the intervention.

Using a transhepatic approach and a one-step trocar technique, the gallbladder was punctured under ultrasound guidance at the hepatic attachment of the gallbladder bed while avoiding intrahepatic bile ducts and major vessels. Following successful access, an 8.5-Fr pigtail catheter (Cook Medical, Bloomington, IN, USA) was placed for drainage. Bile was aspirated and submitted for bacterial culture and antimicrobial susceptibility testing using the BacT/ALERT 3D microbial detection system (bioMérieux, Marcy-l'Étoile, France) and VITEK 2 Compact system (bioMérieux, Marcy-l'Étoile, France). The catheter was then secured and connected to a sterile drainage bag. After the procedure, drainage output and characteristics were recorded routinely, and patients were monitored for vital signs.

Data Collection

The following clinical data were retrospectively collected:

(1) General demographic data: Age, sex, body mass index (BMI).

(2) Underlying diseases: Diabetes mellitus, hypertension, coronary heart disease, chronic kidney disease (CKD), cerebrovascular disease, etc. CCI and ASA classifications were calculated.

(3) Acute cholecystitis-related data: Time from onset to admission (defined as the time interval from the patient's self-reported first occurrence of right upper abdominal pain or fever to hospital admission), TG18 severity grading, gallbladder stone status, gallbladder wall thickness, and pericholecystic fluid collection.

(4) Vital signs at admission: Temperature, heart rate, respiratory rate, and mean arterial pressure (MAP).

(5) Laboratory parameters: First test results within 24 hours before PTGBD, including white blood cell count (WBC), neutrophil percentage, hemoglobin, platelet count, CRP, procalcitonin (PCT), albumin, total bilirubin, direct bilirubin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), serum creatinine, prothrombin time (PT), and INR. White blood cell count and related hematological parameters were measured using an XN-1000 automated hematology analyzer (Sysmex Corporation, Kobe, Japan). Coagulation parameters, including PT and INR, were measured using a STA Compact Max coagulation analyzer (Diagnostica Stago, Asnières-sur-Seine, France). PCT was measured using an electrochemiluminescence immunoassay on a Cobas e801 analyzer (Roche Diagnostics, Basel, Switzerland).

(6) Pain assessment: Visual Analogue Scale (VAS) was used, with scores ranging from 0 to 10, where 0 indicates no pain and 10 indicates severe pain. VAS scores were recorded at admission (baseline), before PTGBD, and at 24 hours, 48 hours, and 72 hours after PTGBD.

(7) Treatment-related parameters: Time from onset to PTGBD, antibiotic use (including empirical antibiotic regimen and adjustments based on susceptibility results), and bile culture results.

(8) Outcome measures: Time to clinical symptom relief after PTGBD, changes in inflammatory markers, drainage-related complications, length of hospital stay, 30-day readmission rate, elective cholecystectomy within 6 months after discharge, and 30-day mortality.

Calculation of CRP/Albumin Ratio

CRP-to-albumin ratio (CAR) = serum CRP (mg/L) / serum albumin (g/L). The first CRP and albumin values measured within 24 hours before PTGBD were used for calculation. CRP was detected using an immunoturbidimetric assay on a Cobas c702 automatic biochemical analyzer (Roche Diagnostics, Basel, Switzerland), with CRP reagent kits provided by Roche Diagnostics (Basel, Switzerland), and results were reported in mg/L (normal reference range: 0–8 mg/L). The bromocresol green method was used for albumin detection on the same biochemical analyzer, using albumin assay reagents supplied by Roche Diagnostics (Basel, Switzerland), with results reported in g/L (normal reference range: 35–50 g/L). Routine laboratory tests were performed in the hospital clinical laboratory according to standardized operating procedures and internal quality-control requirements.

Outcome Definitions

Primary Outcome

Poor treatment response to PTGBD was defined as the occurrence of any one of the following conditions: (1) Failure to achieve body temperature reduction below 38.0 °C at any time within 72 hours after PTGBD, with temperature monitored four times daily (06:00, 10:00, 14:00, and 18:00); (2) Inadequate relief of abdominal pain at 72 hours after PTGBD, defined as a reduction in visual analog scale (VAS) score of less than 50% compared with the pre-procedural baseline; (3) Insufficient improvement in inflammatory markers, defined as a white blood cell (WBC) count remaining $\geq 12 \times 10^9$/L and a reduction of less than 25% from baseline at 72 hours after PTGBD; (4) Requirement for emergency cholecystectomy or other surgical interventions (including repeat percutaneous drainage or emergency laparotomy) within 7 days after PTGBD; (5) All-cause mortality within 30 days following PTGBD.

The primary outcome was defined as a composite endpoint. Both the overall incidence of the composite endpoint and the frequencies of individual components were analyzed and reported separately.

Secondary Outcomes

(1) Drainage-related complications, comprising catheter dislodgement (complete or partial displacement of the catheter from the gallbladder), catheter occlusion (marked reduction or cessation of drainage not resolved by flushing), puncture-site bleeding requiring transfusion or interventional management, and bile leakage confirmed by imaging findings or markedly elevated amylase levels in the drainage fluid; (2) 30-day readmission rate due to cholecystitis-related symptoms or complications; (3) Completion of elective cholecystectomy within 6 months after hospital discharge.

Statistical Methods

Statistical analyses were conducted using SPSS version 26.0 (IBM Corp., Armonk, NY, USA) and R software version 4.2.0 (R Foundation for Statistical Computing, Vienna, Austria). Data entry and preliminary checking were performed using Microsoft Excel 2019 (Microsoft Corp., Redmond, WA, USA). Continuous variables were evaluated for normality using the Shapiro–Wilk test. Data following a normal distribution were presented as mean $\pm$ standard deviation and compared between groups using the independent samples *t* test, whereas non-normally distributed variables were expressed as median with interquar-

tile range and analyzed using the Mann–Whitney U test. Categorical variables were summarized as counts with percentages, and compared using the chi-square test or Fisher's exact test, as appropriate.

Receiver operating characteristic (ROC) curve analysis was applied to assess the discriminative performance of the CRP/albumin ratio (CAR) for predicting poor treatment response to PTGBD. The area under the ROC curve (AUC) with corresponding 95% confidence intervals was calculated, and the optimal cutoff value was determined based on the Youden index. Sensitivity, specificity, positive predictive value, and negative predictive value were subsequently derived. Comparisons of AUCs between CAR and individual biomarkers, including CRP and albumin, were performed using the DeLong test. For the analysis of elective laparoscopic cholecystectomy within 6 months after PTGBD, death within 30 days was considered a competing event. Competing risk analysis was performed using the Fine–Gray subdistribution hazard model to estimate the cumulative incidence of elective LC.

Variables showing a p value < 0.10 in univariate analyses were entered into the multivariable logistic regression model. Prior to model construction, multicollinearity among candidate variables was evaluated using variance inflation factors (VIFs). No evidence of problematic collinearity was observed, and the maximum VIF in the final model was 1.84. A backward stepwise selection approach was then applied to identify independent predictors, with results reported as odds ratios and 95% confidence intervals. Based on the final multivariable model, a predictive model was established, and internal validation was conducted using bootstrap resampling (1000 iterations). Model discrimination was quantified using the C-statistic, while calibration was assessed with the Hosmer–Lemeshow goodness-of-fit test and calibration plots.

Patients were stratified into high and low CAR groups according to the identified cutoff value. Time-to-event outcomes related to clinical remission were analyzed using the Kaplan–Meier method, and group differences between were assessed with the log-rank test. All statistical tests were two-sided, and a p value < 0.05 was considered statistically significant.

Results

Patient Characteristics and Grouping

According to the inclusion and exclusion criteria, this study finally included 309 patients with high-risk acute cholecystitis who underwent PTGBD. According to the primary outcome definition, 78 patients (25.2%) developed poor treatment response to PTGBD (poor response group), and 231 patients (74.8%) had good treatment response (good response group).

The distribution of individual components of the composite endpoint in the poor response group is summarized below. Within 72 hours after PTGBD, 41 patients (52.6%) failed to achieve a body temperature below 38.0 °C, 35 patients (44.9%) showed less than a 50% reduction in VAS score, and 38 patients (48.7%) did not reach the target WBC. In addition, 12 patients (15.4%) required emergency surgical intervention within 7 days, and 5 patients (6.4%) died within 30 days. Because these criteria were not mutually exclusive, the sum of individual components exceeded the total number of patients with poor response.

Comparison of General Data Between the Two Groups

There were no statistically significant differences in age, sex, or BMI between the two groups ($p > 0.05$). The prevalence of diabetes mellitus was higher in the poor response group than in the good response group (46.2% vs 32.0%, $p = 0.025$), as was the prevalence of CKD (20.5% vs 10.8%, $p = 0.029$). The CCI and proportion of ASA $\geq$III were both higher in the poor response group than in the good response group ($p < 0.05$) (Table 1).

Comparison of Acute Cholecystitis-Related Data Between the Two Groups

The time from onset to admission was longer in the poor response group than in the good response group [72 (48–96) h vs 48 (24–72) h, $p < 0.001$]. The proportion of TG18 Grade III was higher in the poor response group than in the good response group (52.6% vs 33.3%, $p = 0.003$). The poor response group showed a greater Gallbladder wall thickness ($p = 0.001$) and a higher proportion of pericholecystic fluid collection ($p = 0.019$) (Table 2).

Comparison of Baseline Vital Signs and Laboratory Parameters Between the Two Groups

At admission, patients in the poor response group presented with a more pronounced systemic inflammatory and hemodynamic disturbance. Body temperature and heart rate were significantly higher in the poor response group compared with the good response group (both $p < 0.01$), whereas mean arterial pressure was lower ($p = 0.016$). No significant difference was observed in respiratory rate between the two groups. Baseline laboratory parameters before PTGBD further reflected a more severe inflammatory and metabolic burden in the poor response group. WBC, neutrophil percentage, CRP, PCT, liver function indices (total bilirubin, direct bilirubin, ALT, and AST), renal function (serum creatinine), and coagulation parameters (PT and INR) were all significantly elevated in the poor response group (all $p < 0.05$). In contrast, serum albumin levels were significantly lower in the poor response group ($p < 0.001$). Hemoglobin and platelet counts did not differ significantly between groups ($p > 0.05$) (Table 3).

Table 1. Comparison of general demographic data and underlying diseases between the two groups.

Variable	Good Response Group (n = 231)	Poor Response Group (n = 78)	t/χ^2/Z value	p value
Age (years, $\bar{x} \pm s$)	68.4 ± 12.3	70.2 ± 11.8	$t = -1.147$	0.252
Male [n (%)]	128 (55.4)	48 (61.5)	$\chi^2 = 0.896$	0.344
BMI (kg/m^2, $\bar{x} \pm s$)	24.2 ± 3.5	24.6 ± 3.8	$t = -0.842$	0.4
Diabetes mellitus [n (%)]	74 (32.0)	36 (46.2)	$\chi^2 = 4.987$	0.025
Hypertension [n (%)]	112 (48.5)	43 (55.1)	$\chi^2 = 1.032$	0.31
Coronary heart disease [n (%)]	45 (19.5)	19 (24.4)	$\chi^2 = 0.834$	0.361
Chronic kidney disease [n (%)]	25 (10.8)	16 (20.5)	$\chi^2 = 4.752$	0.029
Cerebrovascular disease [n (%)]	32 (13.9)	14 (17.9)	$\chi^2 = 0.756$	0.385
CCI [M (IQR)] (points)	3 (2–4)	4 (3–5)	Z = –3.526	<0.001
ASA ≥III [n (%)]	156 (67.5)	63 (80.8)	$\chi^2 = 4.823$	0.028

Notes: BMI, body mass index; CCI, Charlson Comorbidity Index; ASA, American Society of Anesthesiologists classification.

Table 2. Comparison of acute cholecystitis-related data between the two groups.

Variable	Good Response Group (n = 231)	Poor Response Group (n = 78)	t/χ^2/Z value	p value
Time from onset to admission [M (IQR)] (h)	48 (24–72)	72 (48–96)	Z = –4.235	<0.001
TG18 grading [n (%)]			$\chi^2 = 8.694$	0.003
Grade II	154 (66.7)	37 (47.4)		
Grade III	77 (33.3)	41 (52.6)		
Gallbladder stones [n (%)]	198 (85.7)	69 (88.5)	$\chi^2 = 0.378$	0.539
Gallbladder wall thickness (mm, $\bar{x} \pm s$)	5.8 ± 1.6	6.5 ± 1.8	$t = -3.247$	0.001
Pericholecystic fluid collection [n (%)]	78 (33.8)	38 (48.7)	$\chi^2 = 5.543$	0.019

Note: TG18, Tokyo Guidelines 2018.

Table 3. Baseline vital signs and laboratory parameters before PTGBD.

Variable	Good Response Group (n = 231)	Poor Response Group (n = 78)	t/Z value	p value
Vital signs				
Temperature (°C)	38.2 ± 0.7	38.6 ± 0.8	–4.186	<0.001
Heart rate (beats/min)	92.4 ± 15.6	98.7 ± 17.2	–3.024	0.003
Respiratory rate (breaths/min)	19.2 ± 3.1	19.8 ± 3.4	–1.428	0.154
Mean arterial pressure (mmHg)	86.5 ± 12.4	82.3 ± 13.8	2.424	0.016
Hematological and inflammatory markers				
WBC ($\times 10^9$/L, $\bar{x} \pm s$)	13.8 ± 4.2	16.5 ± 5.1	–4.568	<0.001
Hemoglobin (g/L, $\bar{x} \pm s$)	126.5 ± 18.4	123.8 ± 19.2	1.098	0.273
Platelet count ($\times 10^9$/L, $\bar{x} \pm s$)	198.6 ± 72.4	189.3 ± 78.5	0.956	0.340
Neutrophil percentage (%, $\bar{x} \pm s$)	82.4 ± 7.5	86.2 ± 6.8	–4.012	<0.001
CRP [M (IQR)] (mg/L)	86.5 (45.2–142.3)	168.4 (108.6–238.5)	–6.872	<0.001
PCT [M (IQR)] (ng/mL)	1.2 (0.4–3.8)	3.6 (1.2–8.5)	–5.234	<0.001
Nutritional status				
Albumin (g/L, $\bar{x} \pm s$)	32.4 ± 4.8	28.6 ± 5.2	5.867	<0.001
Liver function				
Total bilirubin [M (IQR)] (μmol/L)	28.5 (18.2–42.6)	38.6 (24.5–58.4)	–3.456	<0.001
Direct bilirubin [M (IQR)] (μmol/L)	12.4 (6.8–22.5)	18.6 (10.2–32.4)	–3.125	0.002
ALT [M (IQR)] (U/L)	42.5 (24.6–78.4)	58.6 (32.4–98.5)	–2.856	0.004
AST [M (IQR)] (U/L)	38.4 (22.5–68.6)	52.4 (28.6–86.5)	–2.645	0.008
Renal and coagulation parameters				
Serum creatinine [M (IQR)] (μmol/L)	78.5 (62.4–98.6)	92.4 (72.5–128.6)	–3.524	<0.001
PT (s, $\bar{x} \pm s$)	12.8 ± 1.6	13.5 ± 1.9	–3.124	0.002
INR ($\bar{x} \pm s$)	1.08 ± 0.12	1.14 ± 0.15	–3.456	<0.001

Notes: Values are presented as mean ± standard deviation or median (interquartile range), as appropriate. WBC, white blood cell count; CRP, C-reactive protein; PCT, procalcitonin; ALT, alanine aminotransferase; AST, aspartate aminotransferase; PT, prothrombin time; INR, international normalized ratio; PTGBD, percutaneous transhepatic gallbladder drainage.

Table 4. Comparison of CAR and pain VAS scores between the two groups.

Variable	Good Response Group (n = 231)	Poor Response Group (n = 78)	Z value	*p* value
CAR [M (IQR)]	2.68 (1.35–4.52)	5.82 (3.65–8.96)	–7.524	<0.001
VAS score (points)				
At admission [M (IQR)]	7 (6–8)	7 (6–8)	–0.856	0.392
Before PTGBD [M (IQR)]	6 (5–7)	6 (5–8)	–1.245	0.213
24 h post-procedure [M (IQR)]	4 (3–5)	5 (4–6)	–4.568	<0.001
48 h post-procedure [M (IQR)]	2 (2–3)	4 (3–5)	–6.856	<0.001
72 h post-procedure [M (IQR)]	1 (1–2)	3 (2–4)	–7.234	<0.001

Notes: CAR, CRP/albumin ratio; VAS, Visual Analogue Scale; PTGBD, percutaneous transhepatic gallbladder drainage.

Table 5. Comparison of dynamic changes in inflammatory markers after PTGBD between the two groups.

Variable	Good Response Group (n = 231)	Poor Response Group (n = 78)	Z value	*p* value
CRP [M (IQR)] (mg/L)				
Pre-procedure (baseline)	86.5 (45.2–142.3)	168.4 (108.6–238.5)	–6.872	<0.001
24 h post-procedure	68.4 (35.6–118.5)	152.6 (98.4–225.6)	–6.524	<0.001
48 h post-procedure	45.2 (22.4–82.6)	128.5 (78.6–198.4)	–7.125	<0.001
72 h post-procedure	32.5 (15.8–58.4)	105.6 (62.4–168.5)	–7.456	<0.001
CRP decrease from baseline [M (IQR)] (%)	62.4 (48.5–72.6)	37.3 (22.8–52.4)	–8.856	<0.001
PCT [M (IQR)] (ng/mL)				
Pre-procedure (baseline)	1.2 (0.4–3.8)	3.6 (1.2–8.5)	–5.234	<0.001
24 h post-procedure	0.9 (0.3–2.8)	3.2 (1.0–7.6)	–5.124	<0.001
48 h post-procedure	0.6 (0.2–1.8)	2.6 (0.8–6.2)	–5.456	<0.001
72 h post-procedure	0.4 (0.1–1.2)	2.1 (0.6–5.4)	–5.867	<0.001
PCT decrease from baseline [M (IQR)] (%)	66.7 (52.4–76.8)	41.7 (28.5–55.6)	–7.645	<0.001

Notes: Decrease rate = (baseline value – 72 h post-procedure value) / baseline value × 100%; expressed as median (interquartile range) due to skewed distribution; PTGBD, percutaneous transhepatic gallbladder drainage; CRP, C-reactive protein; PCT, procalcitonin.

Comparison of CAR and Pain Scores Between the Two Groups

CAR was higher in the poor response group than in the good response group [5.82 (3.65–8.96) vs 2.68 (1.35–4.52), $p < 0.001$]. There were no statistically significant differences in VAS scores at admission or before PTGBD between the two groups ($p > 0.05$). VAS scores at 24 h, 48 h, and 72 h after PTGBD were all higher in the poor response group than in the good response group ($p < 0.001$) (Table 4).

Comparison of Dynamic Changes in Inflammatory Markers After PTGBD Between the Two Groups

To evaluate the trend of inflammatory response changes after PTGBD, serum CRP and PCT levels were monitored in both groups at 24 h, 48 h, and 72 h postoperatively. Results showed that CRP and PCT levels decreased in both groups from baseline, but the decrease was more pronounced in the good response group. The rate of CRP decrease from baseline at 72 h post-procedure was significantly higher in the good response group than in the poor response group [62.4 (48.5–72.6)% vs 37.3 (22.8–52.4)%, $p < 0.001$], as was the rate of PCT decrease from baseline [66.7 (52.4–76.8)% vs 41.7 (28.5–55.6)%, $p < 0.001$] (Table 5).

Comparison of Treatment-Related Parameters Between the Two Groups

The time from onset to PTGBD was longer in the poor response group than in the good response group ($p < 0.001$). The bile culture positivity rate was higher in the poor response group than in the good response group ($p = 0.018$), and the proportion of antibiotic regimen adjustment was higher in the poor response group ($p = 0.021$) (Table 6).

Predictive Value of CAR for Poor Treatment Response to PTGBD

ROC curve analysis showed that the AUC of CAR for predicting poor treatment response to PTGBD was 0.812 (95% CI: 0.758–0.866), which was higher than that of CRP (AUC = 0.756, 95% CI: 0.695–0.817) and albumin (AUC = 0.718, 95% CI: 0.654–0.782) ($p < 0.05$). The optimal cutoff value of CAR was 3.85, with a sensitivity of 74.4%, specificity of 76.2%, PPV of 51.3%, and NPV of 89.8% (Table 7, Fig. 1).

Multivariable Logistic Regression Analysis of Poor Treatment Response to PTGBD

To clarify the rationale for variable selection, univariate logistic regression analysis was initially conducted for all candidate variables. Variables with a p value < 0.10 in

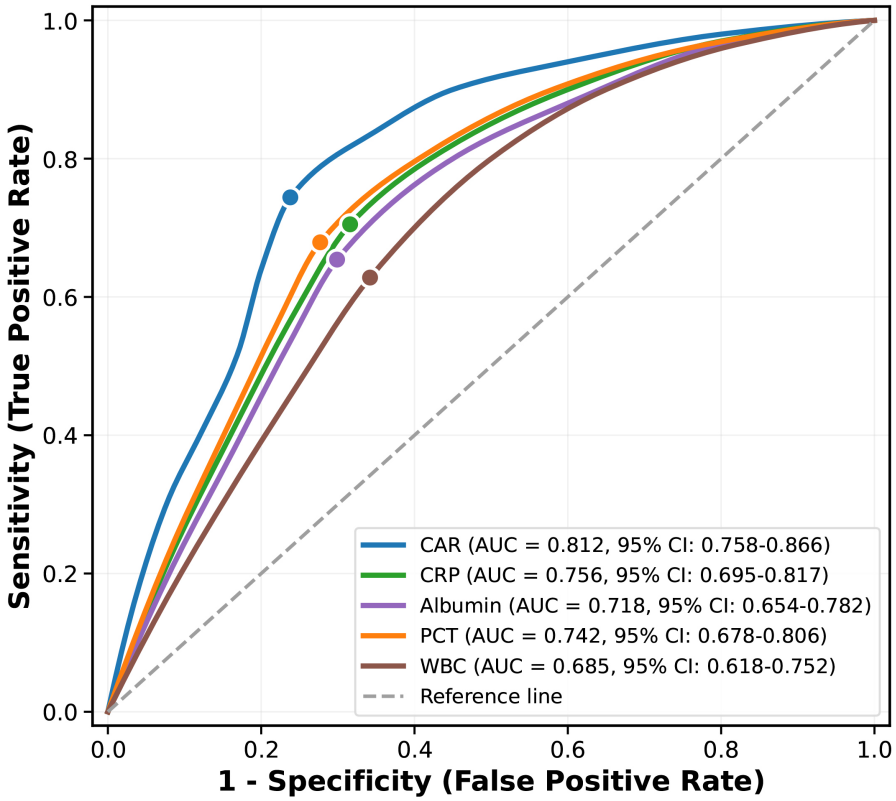

Fig. 1. ROC curves for predicting poor response to PTGBD. ROC, Receiver operating characteristic; PTGBD, percutaneous transhepatic gallbladder drainage.

Table 6. Comparison of treatment-related parameters between the two groups.

Variable	Good Response Group (n = 231)	Poor Response Group (n = 78)	χ^2/Z value	*p* value
Time from onset to PTGBD [M (IQR)] (h)	56 (32–80)	84 (56–108)	Z = –4.856	<0.001
Empirical antibiotic regimen [n (%)]			χ^2 = 1.245	0.537
Ceftriaxone	142 (61.5)	44 (56.4)		
Piperacillin–tazobactam	68 (29.4)	28 (35.9)		
Others	21 (9.1)	6 (7.7)		
Antibiotic regimen adjustment [n (%)]	52 (22.5)	28 (35.9)	χ^2 = 5.324	0.021
Positive bile culture [n (%)]	98 (42.4)	45 (57.7)	χ^2 = 5.567	0.018
Main cultured organisms [n (%)]*				
Escherichia coli	48 (49.0)	22 (48.9)	χ^2 = 0.001	0.997
Klebsiella pneumoniae	24 (24.5)	12 (26.7)	χ^2 = 0.078	0.780
Enterococcus spp.	15 (15.3)	8 (17.8)	χ^2 = 0.136	0.712
Others	11 (11.2)	3 (6.7)	χ^2 = 0.722	0.396

Notes: *Proportion among patients with positive culture; PTGBD, percutaneous transhepatic gallbladder drainage.

the univariate analysis were subsequently entered into the multivariable logistic regression model. In the univariate analysis, CAR ≥3.85, TG18 Grade III, time from onset to PTGBD ≥72 h, diabetes mellitus, and CCI ≥4 were significantly associated with poor treatment response, whereas age and sex did not meet the predefined inclusion criterion. Collinearity diagnostics revealed no evidence of significant multicollinearity among the variables included in the multivariable model, with a maximum VIF of 1.84. Multivariable logistic regression analysis further demonstrated CAR ≥3.85, TG18 Grade III, delayed PTGBD (≥72 h), diabetes mellitus, and CCI ≥4 as independent risk factors for poor treatment response to PTGBD (Table 8).

Construction and Validation of the Prediction Model

A prediction model was constructed based on the multivariable analysis results. Bootstrap internal validation (1000 resamples) showed a C-statistic of 0.798 (95% CI: 0.742–0.854). The Hosmer-Lemeshow test indicated good model calibration (χ^2 = 6.524, p = 0.589). The calibration

Table 7. ROC curve analysis of CAR and related indicators for predicting poor treatment response to PTGBD.

Indicator	AUC (95% CI)	Optimal Cutoff	Sensitivity (%)	Specificity (%)	PPV (%)	NPV (%)	*p* value*
CAR	0.812 (0.758–0.866)	3.85	74.4	76.2	51.3	89.8	-
CRP (mg/L)	0.756 (0.695–0.817)	125.6	70.5	68.4	43	87.3	0.024
Albumin (g/L)	0.718 (0.654–0.782)	≤30.2	65.4	70.1	42.5	85.6	0.003
PCT (ng/mL)	0.742 (0.678–0.806)	2.45	67.9	72.3	45.3	86.8	0.016
WBC ($\times 10^9$/L)	0.685 (0.618–0.752)	14.8	62.8	65.8	38.3	83.9	<0.001

Notes: *DeLong test *p* value compared with CAR; Albumin is a protective factor, cutoff ≤30.2 g/L predicts poor response; AUC, area under the curve; CI, confidence interval; PPV, positive predictive value; NPV, negative predictive value; CAR, CRP/albumin ratio; CRP, C-reactive protein; PCT, procalcitonin; WBC, white blood cell count; PTGBD, percutaneous transhepatic gallbladder drainage.

Table 8. Univariate and multivariable logistic regression analysis of poor treatment response to PTGBD.

Variable	Univariate OR (95% CI)	*p* value	Multivariable OR (95% CI)	*p* value
CAR ≥3.85	3.96 (2.31–6.78)	<0.001	3.42 (1.89–6.18)	<0.001
TG18 Grade III	2.64 (1.55–4.50)	<0.001	2.28 (1.26–4.12)	0.006
Time from onset to PTGBD ≥72 h	2.48 (1.49–4.14)	0.001	2.15 (1.18–3.92)	0.012
Diabetes mellitus	2.05 (1.22–3.46)	0.007	1.86 (1.04–3.33)	0.036
CCI ≥4	2.21 (1.32–3.69)	0.003	1.92 (1.08–3.41)	0.026

Notes: Variables with $p < 0.10$ in univariate analysis were entered into the multivariable logistic regression model. OR, odds ratio; CI, confidence interval; CAR, C-reactive protein/albumin ratio; TG18, Tokyo Guidelines 2018; PTGBD, percutaneous transhepatic gallbladder drainage; CCI, Charlson Comorbidity Index.

curve showed a good agreement between predicted probability and actual incidence (Fig. 2).

Comparison of Clinical Remission Time Between the High CAR and Low CAR Groups

According to the optimal CAR cutoff value of 3.85, patients were classified into a high CAR group (CAR ≥3.85, n = 113) and a low CAR group (CAR <3.85, n = 196). Because remission time variables were non-normally distributed, between-group comparisons were performed using the Mann–Whitney U test. The time to temperature normalization was significantly longer in the high CAR group than in the low CAR group [72 (48–96) h vs 48 (24–72) h; Z = –4.87, $p < 0.001$]. Similarly, patients in the high CAR group showed prolonged time to abdominal pain relief [96 (72–120) h vs 48 (36–72) h; Z = –5.12, $p < 0.001$] and delayed normalization of WBC [96 (72–144) h vs 72 (48–96) h; Z = –4.53, $p < 0.001$], compared with those in the low CAR group. Kaplan–Meier analysis further demonstrated that the cumulative clinical remission curve of the high CAR group was consistently lower than that of the low CAR group, indicating a slower remission process in patients with elevated CAR (log-rank $\chi^2 = 28.456$, $p < 0.001$) (Fig. 3).

Comparison of Outcome Measures Between the Two Groups

Length of hospital stay was significantly longer in the poor response group than in the good response group [14 (10–18) d vs 9 (7–12) d, $p < 0.001$]. The poor response group also exhibited a higher incidence of drainage-related complications (16.7% vs 7.8%, $p = 0.024$) and a higher 30-day readmission rate (12.8% vs 5.2%, $p = 0.022$). Regarding subsequent surgical management, the crude completion rate of elective laparoscopic cholecystectomy within 6 months after PTGBD was lower in the poor response group than in the good response group (48.7% vs 68.4%, $p = 0.002$). When death within 30 days was considered a competing event, the 6-month cumulative incidence of elective cholecystectomy remained lower in the poor response group than in the good response group (49.8% vs 66.9%). Fine–Gray competing risk analysis showed that poor treatment response was associated with a lower subdistribution hazard for elective cholecystectomy within 6 months (SHR = 0.63, 95% CI: 0.42–0.95, $p = 0.028$) (Table 9).

Discussion

In this retrospective cohort study of 309 patients with high-risk acute cholecystitis undergoing PTGBD, preoperative CAR was identified as an independent predictor of poor treatment response and demonstrated superior discriminative ability compared with CRP or albumin alone. Using a cutoff value of 3.85, CAR achieved an AUC of 0.812, indicating a favorable balance between sensitivity and specificity in predicting early treatment failure after drainage. These findings suggest that CAR may serve as a clinically useful indicator for early risk stratification in this vulnerable patient population.

Acute cholecystitis remains a common surgical emergency, and management decisions in high-risk patients are often constrained by advanced age, multiple comorbidities, and limited physiological reserve. For such patients, PTGBD has been widely recommended as an alternative or

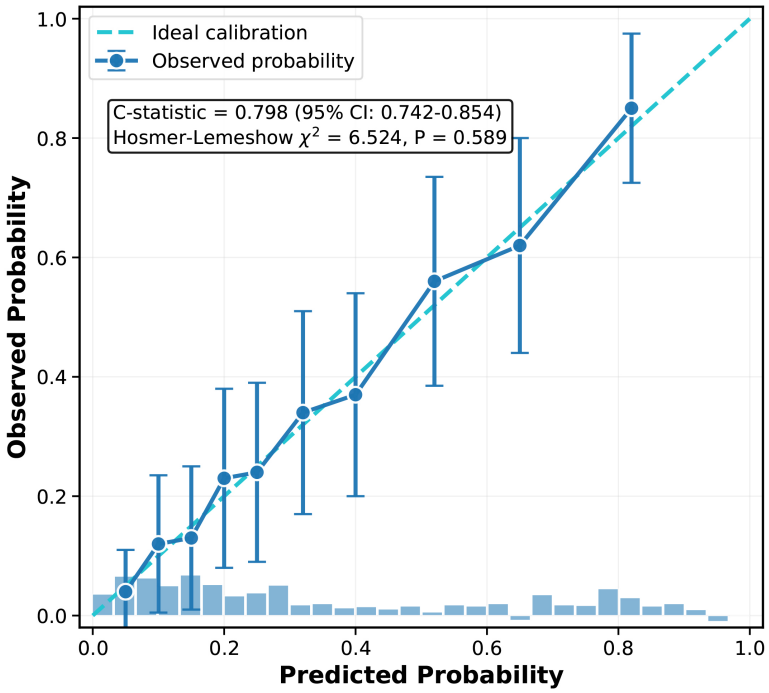

Fig. 2. Calibration curve of the prediction model.

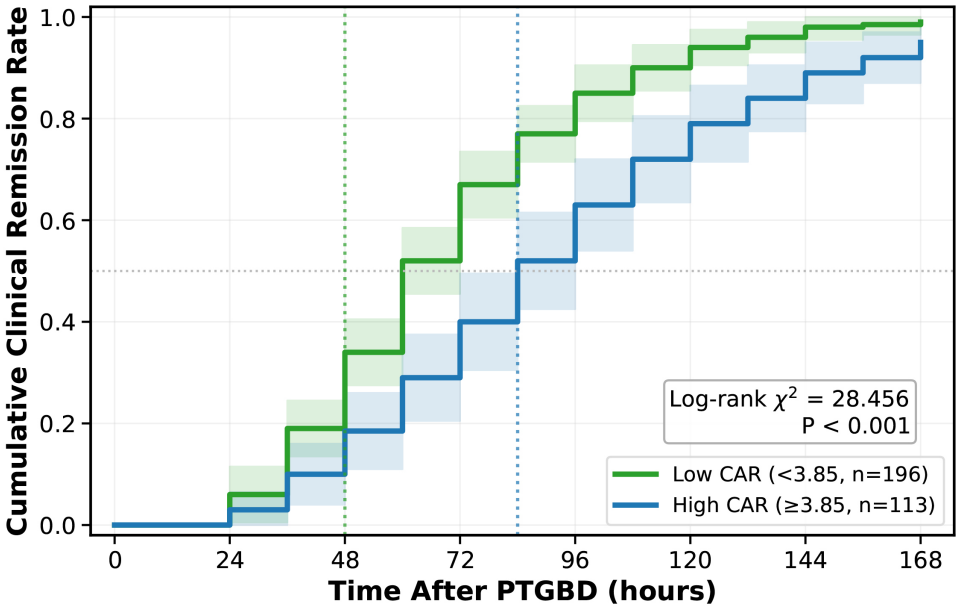

Fig. 3. Kaplan-meier curves for clinical remission time by CAR level. Cumulative clinical remission rate was defined as the proportion of patients who achieved overall clinical remission, indicated by normalization of body temperature (<38.0 °C), relief of abdominal pain, and normalization of white blood cell count, without the need for emergency surgical intervention or death. Time was calculated from PTGBD to the first occurrence of clinical remission. Differences between groups were compared using the log-rank test. CAR, C-reactive protein/albumin ratio.

bridging strategy to emergency cholecystectomy by current guidelines [10,11]. Nevertheless, drainage does not uniformly result in satisfactory clinical improvement. In the present study, approximately one quarter of patients experienced a poor response following PTGBD, which is consistent with previously reported rates ranging from 20% to 30% [12]. Early identification of patients at increased risk of treatment failure is therefore of considerable importance for optimizing monitoring intensity and guiding subsequent therapeutic decisions.

Table 9. Comparison of outcome measures between the two groups.

Variable	Good Response Group (n = 231)	Poor Response Group (n = 78)	χ^2/Z value	*p* value
Length of hospital stay [M (IQR)] (d)	9 (7–12)	14 (10–18)	Z = –5.867	<0.001
Drainage-related complications [n (%)]	18 (7.8)	13 (16.7)	χ^2 = 5.124	0.024
Catheter dislodgement	8 (3.5)	5 (6.4)		
Catheter occlusion	6 (2.6)	4 (5.1)		
Puncture site bleeding	3 (1.3)	3 (3.8)		
Bile leak	1 (0.4)	1 (1.3)		
30-day readmission [n (%)]	12 (5.2)	10 (12.8)	χ^2 = 5.234	0.022
Crude elective LC within 6 months [n (%)]	158 (68.4)	38 (48.7)	χ^2 = 9.736	0.002
6-month CIF of elective LC (%)	66.9	49.8	Gray's test χ^2 = 4.81	0.028
Competing risk analysis (poor vs good response)	—	SHR = 0.63 (95% CI: 0.42–0.95)	Z = –2.20	0.028
30-day mortality [n (%)]	0 (0)	5 (6.4)	Fisher's exact test	0.002

Notes: LC, laparoscopic cholecystectomy; CIF, cumulative incidence function; SHR, subdistribution hazard ratio. Death within 30 days after PTGBD was considered a competing event in the analysis of elective LC within 6 months.

A study has explored various inflammatory or nutritional markers in acute cholecystitis and related intra-abdominal infections, primarily focusing on disease severity, surgical difficulty, or postoperative outcomes [9]. CRP is a well-established acute-phase reactant reflecting systemic inflammation, but its prognostic value may be limited when used in isolation due to susceptibility to multiple confounding factors [13]. Serum albumin, on the other hand, reflects nutritional and immunological status and is frequently reduced in patients with severe infection, partly as a result of increased vascular permeability, enhanced protein catabolism, and impaired hepatic synthesis [14,15]. In recent years, composite indices integrating inflammatory and nutritional parameters have been increasingly recognized as more comprehensive indicators of host response and disease burden [16].

CAR reflects both systemic inflammatory activity and nutritional–immune status, and its prognostic relevance has been documented in various infectious and critical illness settings, including sepsis and severe pneumonia [17]. However, most prior studies have primarily focused on overall prognosis or mortality rather than short-term treatment response. In the present study, attention was directed specifically to clinical response following PTGBD in high-risk patients with acute cholecystitis, and CAR demonstrated superior predictive performance compared with CRP or albumin alone, consistent with observations reported in other intra-abdominal infections [18]. A plausible explanation is that elevated CAR captures the combined effects of pronounced inflammation and impaired nutritional reserve, which may compromise host defense and tissue repair capacity, thereby delaying inflammatory resolution after drainage. Recent high-level evidence has further strengthened this concept; a pooled analysis published in 2024 evaluating CAR in biliary interventional therapies showed that higher CAR values were consistently associated with unfavorable outcomes across multiple centers and diverse patient populations. Although that analysis primarily focused on long-term prognosis and included heterogeneous biliary interventions, its conclusions are directionally aligned with our findings. In comparison, the present study provides a more focused assessment of early treatment response after PTGBD in a well-defined, high-risk acute cholecystitis cohort, extending the clinical applicability of CAR to a specific and challenging therapeutic context.

In addition to CAR, TG18 Grade III disease and delayed drainage (≥72 hours from symptom onset) were independently associated with poor treatment response. Patients with severe acute cholecystitis often present with pronounced local inflammatory changes, gallbladder ischemia, gangrenous transformation, or perforation, conditions in which percutaneous drainage alone may be less effective in achieving rapid disease control, as previously reported [19]. Prolonged delay before PTGBD may further exacerbate infection and inflammatory mediator release, increasing the risk of systemic inflammatory response syndrome [20]. Consistent with previous reports, earlier drainage has been associated with improved outcomes compared with delayed intervention [21]. Diabetes mellitus and a higher Charlson Comorbidity Index also emerged as relevant risk factors, likely reflecting impaired immune defense, microvascular dysfunction, and reduced physiological reserve in these patients [22,23].

Dynamic assessment of postoperative inflammatory markers provided additional insight into treatment response. Although both CRP and PCT declined after PTGBD, the magnitude of reduction at 72 hours was significantly greater in patients with a good response, suggesting that the tempo of inflammatory resolution is closely related to clinical improvement. This observation is consistent with earlier studies indicating that changes in inflammatory markers within 48–72 hours after drainage may have prognostic value [24]. Moreover, a higher bile culture positivity rate in the poor response group may reflect greater

bacterial burden or more severe infection, further contributing to delayed recovery [25].

The prediction model developed in this study demonstrated acceptable discrimination and calibration on internal validation. Clinically, patients with elevated preoperative CAR experienced longer times to defervescence, pain relief, and normalization of leukocyte counts, as well as prolonged hospitalization and higher rates of drainage-related complications and readmission. These findings suggest that CAR may help clinicians identify patients who require closer surveillance or earlier consideration of alternative or escalated treatment strategies following PTGBD [26].

Several limitations of this study should be acknowledged. This analysis was performed at a single center using a retrospective cohort design, which may have introduced selection bias and limited the generalizability of the findings. Although internal validation indicated a relatively stable predictive performance, the lack of an independent external validation cohort means that the applicability of the model to other clinical settings still requires further confirmation. The study population consisted of consecutively eligible patients during the study period, and the sample size was therefore determined by clinical availability rather than a predefined calculation; while the number of outcome events was sufficient to support the planned analyses, the results should nonetheless be interpreted with appropriate caution. In addition, the cutoff value of the CRP/albumin ratio was derived from the present cohort, and potential variability related to regional characteristics, laboratory measurement methods, and patient heterogeneity cannot be excluded. Furthermore, postoperative inflammatory dynamics were evaluated using serial CRP and PCT measurements, whereas dynamic changes in postoperative CAR were not analyzed, as serum albumin levels are not routinely assessed after PTGBD and may be influenced by peri-procedural fluid management and nutritional support. Finally, given the retrospective nature of the study, certain factors—such as differences in patient compliance, peri-procedural management, and nursing care—were difficult to fully standardize and may have affected clinical outcomes.

Conclusion

In summary, preoperative CAR is an effective indicator for predicting poor treatment response to PTGBD in patients with high-risk acute cholecystitis. CAR $\geq$3.85 indicates a significantly increased risk of poor treatment response. This indicator is convenient to measure and low in cost, facilitating its clinical utility. For patients with elevated CAR, clinicians should strengthen monitoring and early adjustment of treatment strategies when necessary to improve outcomes.

Availability of Data and Materials

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

Author Contributions

CY: Primary research design, data collection and analysis, manuscript drafting, project supervision. AL: Clinical data curation, patient follow-up, statistical analysis, critical revision of the manuscript. JW: Senior investigator responsible for study design, methodology guidance, critical revision of the manuscript, and final approval. All authors have read and agreed to the published version of the manuscript. All authors have participated sufficiently in the work to take public responsibility for appropriate portions of the content and agreed to be accountable for all aspects of the work in ensuring that questions related to its accuracy or integrity.

Ethics Approval and Consent to Participate

This study was a single-center retrospective cohort study and was approved by The Affiliated Hospital of Xuzhou Medical University (Approval No.XYFY2025-K1437-03). Due to the retrospective nature of the study and the use of anonymized clinical data, the requirement for informed consent was waived by the ethics committee. All procedures were conducted in accordance with the Declaration of Helsinki.

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Conflict of Interest

The authors declare no conflict of interest.

References

[1] Li S, Guizzetti L, Ma C, Shaheen AA, Dixon E, Ball C, *et al*. Epidemiology and Outcomes of Symptomatic Cholelithiasis and Cholecystitis in the USA: Trends and Urban-Rural Variations. Journal of Gastrointestinal Surgery: Official Journal of the Society for Surgery of the Alimentary Tract. 2023; 27: 932–944. https://doi.org/10.1007/s11605-023-05604-0.

[2] Park TY, Do JH, Oh HC, Choi YS, Lee SE, Kang H, *et al*. Relationship between the Tokyo Guidelines and Pathological Severity in Acute Cholecystitis. Journal of Personalized Medicine. 2023; 13: 1335. https://doi.org/10.3390/jpm13091335.

[3] Osterman E, Helenius L, Larsson C, Jakobsson S, Majumder T, Blomberg A, *et al*. Surgery for acute cholecystitis in severely

comorbid patients: a population-based study on acute cholecystitis. BMC Gastroenterology. 2022; 22: 371. https://doi.org/10.1186/s12876-022-02453-0.

[4] Cirocchi R, Amato L, Ungania S, Buononato M, Tebala GD, Cirillo B, *et al*. Management of Acute Cholecystitis in High-Risk Patients: Percutaneous Gallbladder Drainage as a Definitive Treatment vs. Emergency Cholecystectomy-Systematic Review and Meta-Analysis. Journal of Clinical Medicine. 2023; 12: 4903. https://doi.org/10.3390/jcm12154903.

[5] Liu YQ, Cai X, Zheng ZX, Xu FJ, Bi JT. Increased difficulty and complications of delayed laparoscopic cholecystectomy following percutaneous transhepatic gallbladder drainage in acute cholecystitis: a retrospective study. BMC Surgery. 2023; 23: 277. https://doi.org/10.1186/s12893-023-02185-2.

[6] Olson ME, Hornick MG, Stefanski A, Albanna HR, Gjoni A, Hall GD, *et al*. A biofunctional review of C-reactive protein (CRP) as a mediator of inflammatory and immune responses: differentiating pentameric and modified CRP isoform effects. Frontiers in Immunology. 2023; 14: 1264383. https://doi.org/10.3389/fimmu.2023.1264383.

[7] Zhang J, Zhao Q, Liu S, Yuan N, Hu Z. Clinical predictive value of the CRP-albumin-lymphocyte index for prognosis of critically ill patients with sepsis in intensive care unit: a retrospective single-center observational study. Frontiers in Public Health. 2024; 12: 1395134. https://doi.org/10.3389/fpubh.2024.1395134.

[8] Giner-Galvañ V, Pomares-Gómez FJ, Quesada JA, Rubio-Rivas M, Tejada-Montes J, Baltasar-Corral J, *et al*. C-Reactive Protein and Serum Albumin Ratio: A Feasible Prognostic Marker in Hospitalized Patients with COVID-19. Biomedicines. 2022; 10: 1393. https://doi.org/10.3390/biomedicines10061393.

[9] Gojayev A, Karakaya E, Erkent M, Yücebaş SC, Aydin HO, Kavasoğlu L, *et al*. A novel approach to distinguish complicated and non-complicated acute cholecystitis: Decision tree method. Medicine. 2023; 102: e33749. https://doi.org/10.1097/MD.0000000000033749.

[10] Coccolini F, Cucinotta E, Mingoli A, Zago M, Altieri G, Biloslavo A, *et al*. Acute cholecystitis management in high-risk, critically ill, and unfit-for-surgery patients: the Italian Society of Emergency Surgery and Trauma (SICUT) guidelines. Updates in Surgery. 2024; 76: 331–343. https://doi.org/10.1007/s13304-023-01729-8.

[11] Curry J, Chervu N, Cho NY, Hadaya J, Vadlakonda A, Kim S, *et al*. Percutaneous cholecystostomy tube placement as a bridge to cholecystectomy for grade III acute cholecystitis: A national analysis. Surgery Open Science. 2024; 18: 6–10. https://doi.org/10.1016/j.sopen.2024.01.006.

[12] Ábrahám S, Tóth I, Benkő R, Matuz M, Kovács G, Morvay Z, *et al*. Surgical outcome of percutaneous transhepatic gallbladder drainage in acute cholecystitis: Ten years' experience at a tertiary care centre. Surgical Endoscopy. 2022; 36: 2850–2860. https://doi.org/10.1007/s00464-021-08573-0.

[13] Dias RF, de Paula ACRB, Hasparyk UG, de Oliveira Rabelo Bassalo Coutinho M, Alderete JRA, Kanjongo JC, *et al*. Use of C-reactive protein to guide the antibiotic therapy in hospitalized patients: a systematic review and meta-analysis. BMC Infectious Diseases. 2023; 23: 276. https://doi.org/10.1186/s12879-023-08255-3.

[14] Lin TY, Hung NK, Hung SC. Association of malnutrition with SARS-CoV-2 vaccine response in patients undergoing hemodialysis. Clinical Nutrition (Edinburgh, Scotland). 2022; 41: 2683–2690. https://doi.org/10.1016/j.clnu.2022.10.011.

[15] Levitt DG, Levitt MD. Human serum albumin homeostasis: a new look at the roles of synthesis, catabolism, renal and gastrointestinal excretion, and the clinical value of serum albumin measurements. International Journal of General Medicine. 2016; 9: 229–255. https://doi.org/10.2147/IJGM.S102819.

[16] Ding P, Lv J, Sun C, Chen S, Yang P, Tian Y, *et al*. Combined systemic inflammatory immunity index and prognostic nutritional index scores as a screening marker for sarcopenia in patients with locally advanced gastric cancer. Frontiers in Nutrition. 2022; 9: 981533. https://doi.org/10.3389/fnut.2022.981533.

[17] Liu Y, Gao Y, Liang B, Liang Z. The prognostic value of C-reactive protein to albumin ratio in patients with sepsis: a systematic review and meta-analysis. The Aging Male: the Official Journal of the International Society for the Study of the Aging Male. 2023; 26: 2261540. https://doi.org/10.1080/13685538.2023.2261540.

[18] Zhou X, Fu S, Wu Y, Guo Z, Dian W, Sun H, *et al*. C-reactive protein-to-albumin ratio as a biomarker in patients with sepsis: a novel LASSO-COX based prognostic nomogram. Scientific Reports. 2023; 13: 15309. https://doi.org/10.1038/s41598-023-42601-4.

[19] Do YA, Yoon CJ, Lee JH, Choi WS, Lee CH. Percutaneous cholecystostomy as a definitive treatment for acute acalculous cholecystitis: clinical outcomes and risk factors for recurrent cholecystitis. The British Journal of Radiology. 2023; 96: 20220943. https://doi.org/10.1259/bjr.20220943.

[20] Nve E, Badia JM, Amillo-Zaragüeta M, Juvany M, Mourelo-Fariña M, Jorba R. Early Management of Severe Biliary Infection in the Era of the Tokyo Guidelines. Journal of Clinical Medicine. 2023; 12: 4711. https://doi.org/10.3390/jcm12144711.

[21] Gao W, Zheng J, Bai JG, Han Z. Effect of surgical timing on postoperative outcomes in patients with acute cholecystitis after delayed percutaneous transhepatic gallbladder drainage. World Journal of Gastrointestinal Surgery. 2024; 16: 3445–3452. https://doi.org/10.4240/wjgs.v16.i11.3445.

[22] Serban D, Balasescu SA, Alius C, Balalau C, Sabau AD, Badiu CD, *et al*. Clinical and therapeutic features of acute cholecystitis in diabetic patients. Experimental and Therapeutic Medicine. 2021; 22: 758. https://doi.org/10.3892/etm.2021.10190.

[23] Bhattacharjee HK, Kaviyarasan MP, Singh KJ, Don Jose K, Suhani S, Joshi M, *et al*. Age adjusted Charlson comorbidity index (a-CCI) AS a tool to predict 30-day post-operative outcome in general surgery patients. ANZ Journal of Surgery. 2023; 93: 132–138. https://doi.org/10.1111/ans.18178.

[24] Tarján D, Szalai E, Lipp M, Verbói M, Kói T, Erőss B, *et al*. Persistently High Procalcitonin and C-Reactive Protein Are Good Predictors of Infection in Acute Necrotizing Pancreatitis: A Systematic Review and Meta-Analysis. International Journal of Molecular Sciences. 2024; 25: 1273. https://doi.org/10.3390/ijms25021273.

[25] Kaplan U, Handler C, Chazan B, Weiner N, Hatoum OA, Yanovskay A, *et al*. The Bacteriology of Acute Cholecystitis: Comparison of Bile Cultures and Clinical Outcomes in Diabetic and Non-Diabetic Patients. World Journal of Surgery. 2021; 45: 2426–2431. https://doi.org/10.1007/s00268-021-06107-2.

[26] Utsumi M, Sakurai Y, Narusaka T, Tokunaga N, Kitada K, Hamano R, *et al*. C-reactive protein to albumin ratio predicts difficult laparoscopic cholecystectomy in patients with acute cholecystitis diagnosed according to the Tokyo Guidelines 2018. Asian Journal of Endoscopic Surgery. 2022; 15: 487–494. https://doi.org/10.1111/ases.13035.