

Preoperative C-Reactive Protein–Albumin–Lymphocyte Index and Related Clinical Factors Associated With Postoperative Complications Following Cholecystectomy in Acute Cholecystitis: A Retrospective Study

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AIM: Laparoscopic cholecystectomy (LC) is the primary treatment for acute cholecystitis (AC), although various postoperative complications may still occur. Inflammatory composite indices have gained increasing attention in surgical risk assessment; among them, the C-reactive protein–albumin–lymphocyte (CALLY) index integrates systemic inflammation, immune function, and nutritional status. This study aimed to investigate the association between preoperative CALLY index and postoperative complications in patients with AC undergoing cholecystectomy.

METHODS: This retrospective cohort study included 330 patients with AC who underwent cholecystectomy at the Department of General Surgery, Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, between January 2015 and December 2024. Patients were categorized according to the occurrence of postoperative complications. Clinical characteristics, perioperative variables, and preoperative laboratory markers were collected. The CALLY index was calculated using C-reactive protein (CRP), albumin, and lymphocyte count. Between-group comparisons, Spearman correlation analysis, receiver operating characteristic (ROC) curve analysis, and logistic regression analyses were performed to examine the associations of the CALLY index and related clinical factors with postoperative complications and to evaluate their discriminative ability.

RESULTS: Among the 330 patients, 83 (25.2%) experienced postoperative complications. Patients with complications were older and had higher rates of diabetes, gallbladder wall thickness ≥ 5 mm, and a history of previous cholecystitis (all $p < 0.001$). Preoperative CRP levels were elevated, whereas albumin, lymphocyte counts, and CALLY index values were lower in the complication group (all $p < 0.001$). ROC analysis demonstrated that the CALLY index had favorable predictive ability (area under the curve [AUC] = 0.720). Multivariate analysis identified age, diabetes, gallbladder wall thickness, history of cholecystitis, American Society of Anesthesiologists Physical Status (ASA-PS) classification, the 2018 Tokyo Guidelines (TG18) grade, and CALLY index as independent predictors of postoperative complications (all $p < 0.05$).

CONCLUSIONS: Preoperative CALLY index is associated with the occurrence of postoperative complications in patients with AC undergoing cholecystectomy. CALLY index may serve as a supplementary preoperative marker for identifying patients with a higher risk of postoperative complications. However, further prospective multicenter studies are needed to validate its clinical applicability.

Keywords: acute cholecystitis; laparoscopic cholecystectomy; CALLY index; postoperative complications; retrospective study

Introduction

Acute cholecystitis (AC) is among the most common acute abdominal emergencies in general surgery, primarily caused by cystic duct obstruction leading to bile stasis and secondary bacterial infection. It typically presents with abrupt onset and rapid progression, accounting for approximately 3–10% of patients admitted for acute abdominal pain [1,2,3]. Without timely intervention, AC may progress to subacute or chronic cholecystitis and lead to severe com-

plications such as gallbladder perforation or pericholecystic abscess, which can seriously impair quality of life and even threaten patient survival [4]. According to the 2018 Tokyo Guidelines (TG18) and recent international consensus statements [5,6], laparoscopic cholecystectomy (LC) is recommended as the preferred treatment for eligible patients with AC because of its minimally invasive nature and favorable postoperative recovery.

Nevertheless, LC during the acute phase of AC has limitations. Severe gallbladder wall edema, impacted stones at the gallbladder neck, and indistinct Calot's triangle anatomy significantly increase surgical difficulty [7,8]. Moreover, establishing a clear operative field in the context of severe inflammation and adhesions is often challenging, increasing the risk of bile duct misidentification and serious complications such as bile leakage [9]. Consequently, patients undergoing LC for AC remain at a rel-

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actively high risk of postoperative complications. Studies have shown that 10–20% of patients may experience local complications such as infection, abscess, or bile fistula, as well as systemic complications including pulmonary infection, deep vein thrombosis, or multi-organ dysfunction [10]. These complications not only prolong hospitalization and increase healthcare costs but may also necessitate unplanned reoperations. Therefore, accurate preoperative identification of patients at high risk of postoperative complications is important for optimizing perioperative management and potentially reducing complication-related adverse outcomes.

Currently, postoperative risk assessment in AC patients largely relies on traditional clinical indicators and imaging features [11,12]. However, conventional indicators typically reflect a single dimension of patient status, limiting their ability to comprehensively evaluate the body's physiological reserve and compensatory capacity under acute inflammatory stress [13]. Imaging findings mainly focus on morphological changes and cannot dynamically assess systemic functional status [14]. In this context, there is growing interest in evaluating the overall physiological state of the patients. Persistent inflammatory activation, a key pathological feature of AC, can exacerbate tissue damage via the release of inflammatory mediators and interfere with postoperative healing, thereby increasing the risk of complications such as infection [15]. Nutritional status reflects metabolic and reparative potential, with malnutrition impairing tissue healing [16]. Immune dysfunction further reduces the ability to eliminate pathogens, adversely affecting postoperative outcomes [17].

Composite inflammation–nutrition indices have recently received considerable attention in surgical risk assessment. The C-reactive protein–albumin–lymphocyte (CALLY) index integrates inflammation, nutrition, and immune function, providing a more comprehensive reflection of the body's compensatory capacity in response to surgical stress [18]. A previous study demonstrated that in patients with obstructive colorectal cancer, a lower preoperative CALLY index was associated with increased intraoperative bleeding and postoperative complications [19]. In gastric cancer patients undergoing gastrectomy, a lower preoperative CALLY index was significantly correlated with poorer overall survival and recurrence-free survival, serving as an independent predictor of adverse postoperative outcomes [20]. Therefore, this study aimed to investigate the association between the preoperative CALLY index and postoperative complications in AC patients undergoing LC, and to determine whether this integrated inflammation–nutrition–immunity marker could contribute to a more comprehensive preoperative evaluation when considered together with established clinical and surgical risk factors.

Methods

Patient Selection

This retrospective cohort study included AC patients who underwent cholecystectomy in the Department of General Surgery, Sir Run Run Shaw Hospital, Zhejiang University School of Medicine, from January 2015 to December 2024. A total of 330 eligible patients were included, of whom 83 (25.2%) developed postoperative complications (Fig. 1).

Inclusion criteria included: (1) Diagnosis of AC confirmed by clinical symptoms, imaging, and postoperative pathology; (2) Underwent laparoscopic cholecystectomy; (3) Completed preoperative blood tests including complete blood count, inflammatory markers, liver and renal function tests; complete clinical, surgical, and postoperative follow-up data; (4) Age ≥ 18 years, any gender.

Exclusion criteria were as follows: (1) Severe pre-existing or irreversible functional impairment or failure of major organs (including the liver, kidneys, heart or lungs); (2) Concurrent malignancy, autoimmune disease, hematologic disorder, or other chronic inflammatory disease; (3) Receipt of anti-inflammatory or immunosuppressive therapy within 1 month before surgery; (4) Pregnant or lactating women; (5) Incomplete clinical, laboratory, or follow-up data preventing analysis.

Patients with TG18 Grade III were not excluded on the basis of their grade alone; none of the patients of this type included in this study had severe pre-existing or irreversible major organ dysfunction or failure.

Data Extraction

Clinical data extraction was conducted in strict accordance with standardized protocols. All data were obtained from the electronic medical records and paper charts of the study participants.

The following variables were included for analysis:

General clinical characteristics: age, sex, body mass index (BMI), diabetes, hypertension, gallbladder wall thickness, history of prior abdominal surgery, history of biliary colic, and previous episodes of cholecystitis.

Preoperative inflammatory and nutritional markers: C-reactive protein (CRP), albumin (ALB), neutrophil count (NEU), lymphocyte count (LY), monocyte count (MONO), and platelet count (PLT). All laboratory measurements were derived from routine preoperative venous blood tests. Peripheral venous blood samples were collected in the early morning after an overnight fast to minimize the influence of dietary factors. Based on these laboratory parameters, the CALLY index was calculated using the formula: $\text{CALLY} = [\text{ALB (g/L)} * \text{LY (10}^9\text{/L)}] / [\text{CRP (mg/L)} * 10]$ [21].

Surgical parameters included timing of surgery within 72 hours of symptom onset, American Society of Anesthesiologists Physical Status (ASA-PS) classification, TG18 grade, operative duration, and intraoperative blood loss.

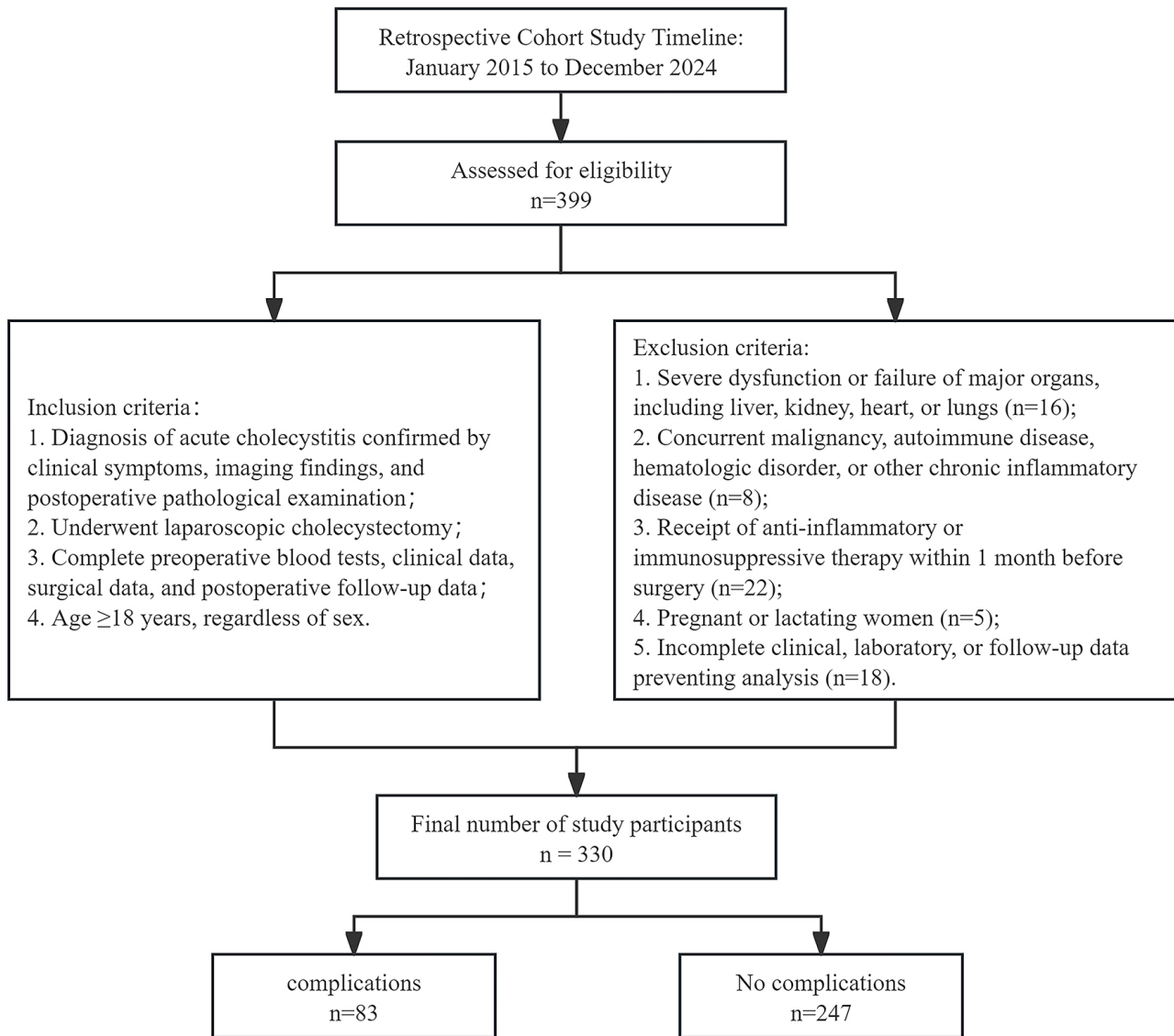


Fig. 1. Study flowchart and participant selection.

Study Outcomes

To objectively assess the severity of complications and enhance clinical interpretability, postoperative adverse events were classified according to the internationally recognized Clavien–Dindo (CD) classification system (Table 1).

In this study, postoperative adverse events of Clavien–Dindo grade II or higher were defined as complications [22]. Patients with one or more CD grade II–V events were uniformly included in the complication group, whereas patients without CD grade II or higher events were included in the non-complication group. The CD classification was used to define and standardize the severity threshold for postoperative complications. Additionally, specific types of complications were analyzed, including bleeding, edema, necrosis, abscess, infection, bile leakage, intestinal obstruction, and ascites [23].

Statistical Analysis

All statistical analyses were performed using R software (version 4.5.1; R Foundation for Statistical Computing, Vienna, Austria), with a significance threshold set at $\alpha = 0.05$; $p < 0.05$ was considered statistically significant. Continuous variables were first assessed for normality using the Shapiro–Wilk test and for homogeneity of variance using Levene’s test. Normally distributed data with equal variance were expressed as mean $\pm$ standard deviation (SD), and intergroup comparisons were conducted using independent-samples *t*-tests. Non-normally distributed data were expressed as median (interquartile range, IQR), with comparisons performed using the Mann–Whitney U test. Categorical variables were presented as counts and percentages (n, %), with intergroup differences analyzed using the chi-square (χ^2) test.

Table 1. Definition of the Clavien–Dindo classification.

CD classifications	Definitions
Grade I	Any deviation from the normal postoperative course without the need for pharmacological treatment or surgical intervention.
Grade II	Complications requiring pharmacological treatment.
Grade IIIa	A complication requiring surgical or radiological intervention rather than general anesthesia.
Grade IIIb	A complication requiring surgical or radiological intervention under general anesthesia.
Grade IVa	A life-threatening complication requiring intensive care management, including single-organ dysfunction.
Grade IVb	A life-threatening complication requiring intensive care management, including multiple organ dysfunction.
Grade V	Death.

Abbreviation: CD, Clavien–Dindo.

After initial two-group comparisons, Spearman correlation analysis was conducted to evaluate associations between preoperative laboratory markers and various types of postoperative complications, clarifying the direction and strength of these relationships and identifying clinically relevant predictive indicators.

Subsequently, receiver operating characteristic (ROC) curve analysis was used to assess the discriminatory ability of CALLY, albumin, lymphocyte counts, and CRP for postoperative complications, thereby evaluating their potential clinical utility in risk assessment.

Variables with statistically significant differences in baseline characteristics were included in univariate logistic regression analysis to identify factors associated with postoperative complications. To reduce multicollinearity and minimize the risk of model overfitting, overlapping individual indicators were excluded. Only statistically significant composite indices and non-overlapping variables from univariate analysis were included in multivariate logistic regression to identify factors independently associated with postoperative complications, with odds ratios (ORs) and 95% confidence intervals (95% CIs) calculated.

Results

General Characteristics and Intraoperative Parameters

Baseline characteristics of the study population are presented in Table 2. Significant differences were observed between the complication and non-complication groups for some variables. Age distribution differed significantly between groups ($p < 0.001$), with a higher proportion of older patients in the complication group. Sex and BMI showed no significant differences ($p > 0.05$).

Among comorbidities, diabetes was more prevalent in the complication group ($p < 0.001$), whereas hypertension did not differ significantly ($p = 0.751$). Gallbladder wall thickness ≥ 5 mm and a history of previous cholecystitis were significantly more common in the complication group (both $p < 0.001$). History of prior abdominal surgery and biliary colic did not differ significantly ($p > 0.05$).

Regarding preoperative inflammatory and nutritional markers, the complication group had higher CRP levels, lower albumin and lymphocyte counts, and significantly reduced CALLY index values (all $p < 0.001$). Neutrophil count,

monocyte count, and platelet count did not differ significantly between groups ($p > 0.05$).

For surgical parameters, the proportion of patients undergoing surgery within 72 hours differed significantly between groups ($p = 0.005$). ASA-PS classification and TG18 grade were higher in the complication group (both $p < 0.001$). Operative duration and intraoperative blood loss showed no significant differences ($p > 0.05$).

Distribution of Postoperative Complications

Among patients who developed postoperative complications (Table 3), the types of complications included edema, abscess, necrosis, bleeding, infection, bile leakage, intestinal obstruction, ascites, and other events. Edema, abscess, and necrosis accounted for the highest proportions, followed by bleeding and infection, whereas bile leakage, intestinal obstruction, and ascites were relatively less common.

Spearman's correlation analysis was performed to evaluate the associations between preoperative inflammatory markers and different types of postoperative complications (Fig. 2). Ascites and other complications were not included in the heatmap because of the limited number of ascites events and the heterogeneous nature of the "Others" category. The CALLY index was negatively correlated with most postoperative complications, particularly edema ($r = -0.55$), necrosis, and abscess, whereas CRP showed positive correlations with most postoperative complications, with the strongest correlation observed for necrosis ($r = 0.60$). In contrast, ALB, LY, PLT, MONO, and NEU showed weaker or inconsistent correlations with specific complications.

ROC curves were constructed based on the overall incidence of postoperative complications to compare the discriminatory ability of the CALLY index with its individual components (Fig. 3). Neutrophil count, monocyte count, and platelet count were not included in the primary ROC comparison because they were not components of the CALLY index and did not differ significantly between patients with and without postoperative complications. The results demonstrated that preoperative CALLY index, albumin, lymphocyte count, and CRP exhibited predictive value for postoperative complications in patients with acute cholecystitis undergoing cholecystectomy. The

Table 2. Baseline clinical characteristics, preoperative laboratory markers, and perioperative parameters of patients.

Variables	No complications (N = 247)	Complications (N = 83)	Statistic	p value
Age, n (%)			$\chi^2 = 32.28$	<0.001
<60 years	191 (77.33)	38 (45.78)		
60–70 years	36 (14.57)	22 (26.51)		
>70 years	20 (8.10)	23 (27.71)		
Sex, n (%)			$\chi^2 = 2.46$	0.117
Female	188 (76.11)	70 (84.34)		
Male	59 (23.89)	13 (15.66)		
BMI (kg/m ²)	22.46 ± 1.89	22.03 ± 1.89	$t = 1.81$	0.072
Diabetes, n (%)	49 (19.84)	33 (39.76)	$\chi^2 = 13.20$	<0.001
Hypertension, n (%)	123 (49.80)	43 (51.81)	$\chi^2 = 0.10$	0.751
Gallbladder wall thickness, n (%)			$\chi^2 = 15.52$	<0.001
<5 mm	175 (70.85)	39 (46.99)		
≥5 mm	72 (29.15)	44 (53.01)		
History of abdominal surgery, n (%)	10 (4.05)	6 (7.23)	$\chi^2 = 0.76$	0.383
History of biliary colic, n (%)	209 (84.62)	74 (89.16)	$\chi^2 = 1.05$	0.306
History of cholecystitis, n (%)	103 (41.70)	52 (62.65)	$\chi^2 = 10.95$	<0.001
Preoperative inflammatory markers				
CRP (mg/L)	9.30 (6.05, 13.85)	13.70 (6.45, 17.70)	$Z = -4.07$	<0.001
Albumin (g/L)	41.40 (38.85, 44.55)	38.90 (36.45, 40.00)	$Z = -5.23$	<0.001
Neutrophils (×10 ⁹ /L)	5.62 (4.29, 7.17)	6.32 (5.19, 7.30)	$Z = -1.59$	0.112
Lymphocyte count (×10 ⁹ /L)	1.93 (1.51, 3.10)	1.57 (1.40, 1.92)	$Z = -4.93$	<0.001
Monocytes (×10 ⁹ /L)	0.49 (0.38, 0.64)	0.55 (0.41, 0.68)	$Z = -1.81$	0.070
Platelet count (×10 ⁹ /L)	236.00 (205.00, 272.00)	231.00 (202.50, 260.50)	$Z = -1.20$	0.231
CALLY index	1.02 (0.57, 1.55)	0.49 (0.30, 0.97)	$Z = -6.00$	<0.001
Surgical parameters				
Surgery within 72 h, n (%)	142 (57.49%)	33 (39.76%)	$\chi^2 = 7.84$	0.005
ASA-PS classification, n (%)			$\chi^2 = 21.54$	<0.001
I–II	198 (80.16)	45 (54.22)		
III–IV	49 (19.84)	38 (45.78)		
TG18 grade, n (%)			$\chi^2 = 27.01$	<0.001
I–II	204 (82.59)	45 (54.22)		
III	43 (17.41)	38 (45.78)		
Operative time (min)	75.71 ± 11.77	78.31 ± 13.18	$t = -1.69$	0.092
Intraoperative blood loss (mL)	159.34 ± 40.96	167.77 ± 41.60	$t = -1.62$	0.107

Abbreviations: BMI, body mass index; CRP, C-reactive protein; CALLY, C-reactive protein–albumin–lymphocyte index; ASA-PS, American Society of Anesthesiologists Physical Status; TG18, 2018 Tokyo Guidelines.

Table 3. Types and distribution of postoperative complications.

Type of complication	Number of cases (n)	Proportion (%)
Bleeding	18	21.69
Edema	28	33.73
Necrosis	20	24.10
Abscess	27	32.53
Infection	16	19.28
Bile leakage	6	7.23
Intestinal obstruction	5	6.02
Ascites	2	2.41
Others	15	18.07

corresponding area under the curve (AUC) values were 0.720 for CALLY, 0.692 for albumin, 0.681 for lymphocyte

count, and 0.649 for CRP, respectively. Among these indicators, the CALLY index showed the best predictive perfor-

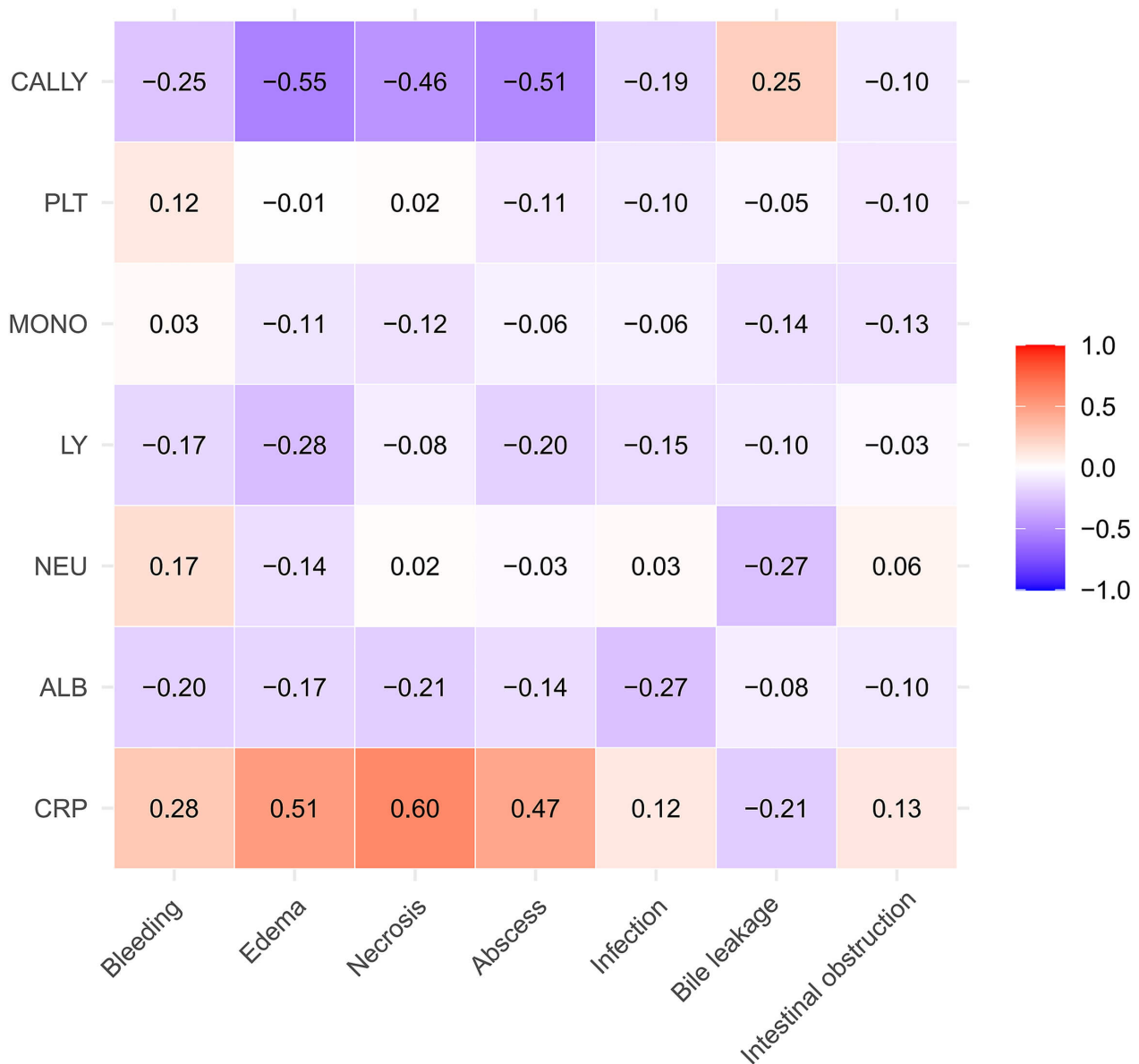


Fig. 2. Correlation analysis between preoperative laboratory markers and postoperative complications. CALLY, C-reactive protein–albumin–lymphocyte; PLT, platelet count; MONO, monocyte count; LY, lymphocyte count; NEU, neutrophil count; ALB, albumin; CRP, C-reactive protein.

mance. According to the Youden index, the optimal cut-off value of the CALLY index was 0.70, with a sensitivity of 65.1%, specificity of 68.8%, and Youden index of 0.339.

Univariate and Multivariate Logistic Regression Analyses

The results of the univariate logistic regression analysis are presented in Table 4. Age stratification was significantly associated with the occurrence of postoperative complications. Compared with patients aged <60 years, those aged 60–70 years and >70 years had significantly increased risks of complications (both $p < 0.001$).

Comorbid diabetes ($p < 0.001$), gallbladder wall thickness ≥ 5 mm ($p < 0.001$), and a history of cholecystitis ($p = 0.001$) were all significantly associated with a higher risk of post-

operative complications. Regarding perioperative assessment indicators, higher ASA-PS classification and TG18 grade III were identified as significant risk factors (both $p < 0.001$). Surgery performed within 72 hours was identified as a protective factor ($p = 0.006$). Among laboratory parameters, higher albumin levels and lymphocyte counts were associated with a reduced risk of complications (both $p < 0.001$), whereas elevated CRP levels were significantly associated with increased risk ($p < 0.001$). A lower CALLY index was also significantly associated with the occurrence of postoperative complications ($p < 0.001$).

Since the CALLY index is derived from albumin, CRP, and lymphocyte count, these individual variables were excluded from the multivariate model to avoid multicollinear-

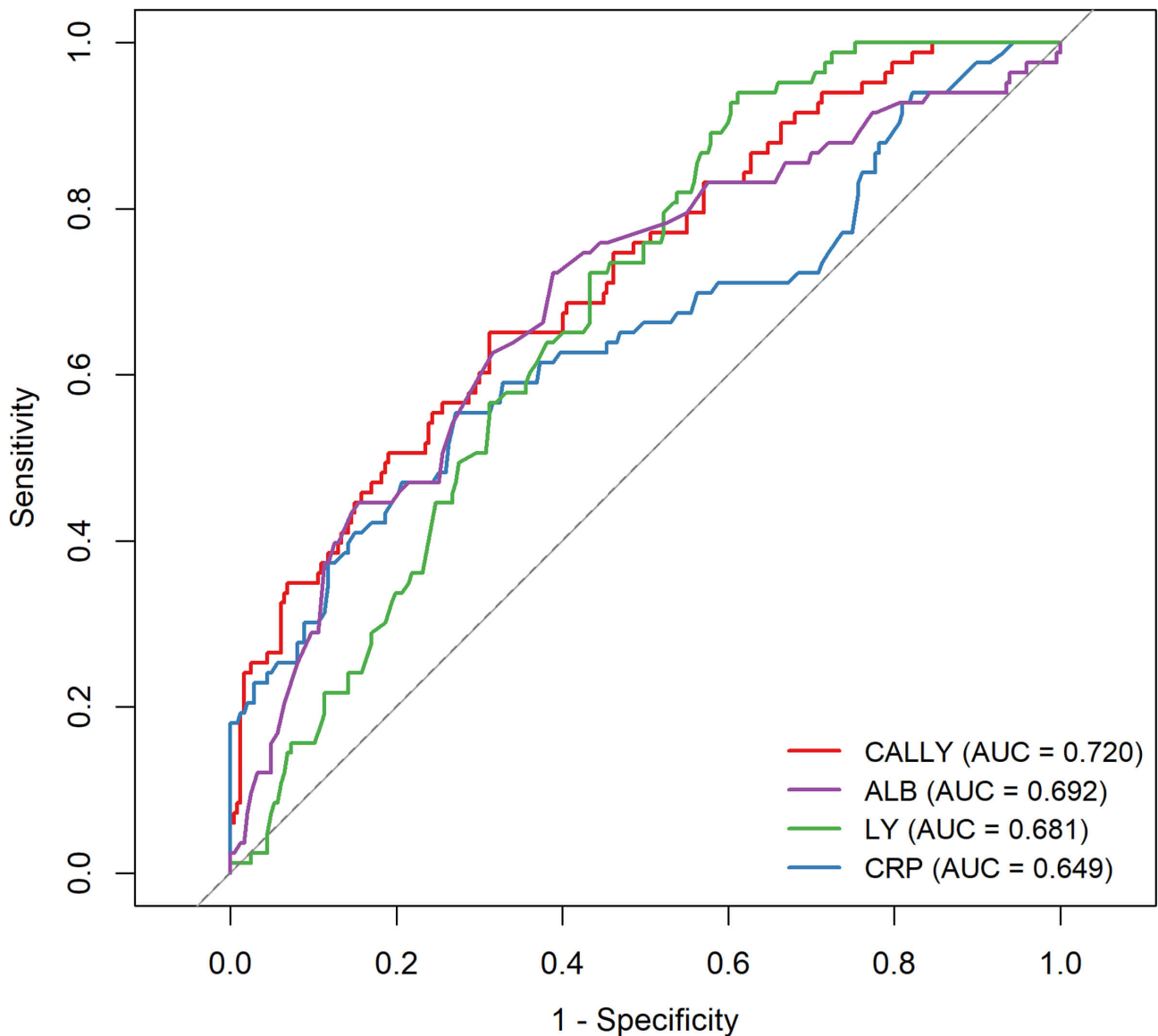


Fig. 3. ROC curves of the CALLY index and its individual components for postoperative complications. ROC, receiver operating characteristic.

ity. Only the composite index and non-overlapping variables were included in the multivariate analysis. The results of the multivariate logistic regression analysis are presented in Table 5. Age remained independently associated with postoperative complications, with significantly increased risks observed in patients aged 60–70 years ($p = 0.003$) and >70 years ($p < 0.001$). Diabetes ($p < 0.001$), gallbladder wall thickness ≥ 5 mm ($p < 0.001$), and a history of cholecystitis ($p < 0.001$) were identified as independent risk factors. Higher ASA-PS classification and TG18 grade III also remained significantly associated with increased complication risk (both $p < 0.001$). Surgery within 72 hours was no longer statistically significant in the multivariate model ($p = 0.627$). Importantly, the CALLY index remained significantly associated with postoperative complications after adjustment for other covariates ($p < 0.001$).

Discussion

In this retrospective cohort study, we evaluated the association between the preoperative CALLY index, related clinical and perioperative factors, and postoperative complications in patients with AC undergoing cholecystectomy. The results showed that a lower CALLY index was significantly associated with an increased risk of postoperative complications and remained independently associated with complications after adjustment for potential confounders. In addition, older age, diabetes, increased gallbladder wall thickness, previous episodes of cholecystitis, higher ASA-PS classification, and higher TG18 grade were also associated with postoperative complications. Although female patients accounted for a relatively high proportion in both groups, sex was not significantly associated with postoperative complications, suggesting that the observed sex dis-

Table 4. Univariate logistic regression analysis of factors associated with postoperative complications.

Variable	β	S.E	Z	p value	OR (95% CI)
Age					
<60 years	—	—	—	—	1.00 (Reference)
60–70 years	1.12	0.32	3.47	<0.001	3.07 (1.63–5.79)
>70 years	1.75	0.35	4.96	<0.001	5.78 (2.89–11.56)
Diabetes					
No	—	—	—	—	1.00 (Reference)
Yes	0.98	0.28	3.56	<0.001	2.67 (1.55–4.57)
Gallbladder wall thickness					
<5 mm	—	—	—	—	1.00 (Reference)
≥ 5 mm	1.01	0.26	3.87	<0.001	2.74 (1.65–4.57)
History of cholecystitis					
No	—	—	—	—	1.00 (Reference)
Yes	0.85	0.26	3.27	0.001	2.35 (1.41–3.91)
ASA-PS classification					
I–II	—	—	—	—	1.00 (Reference)
III–IV	1.23	0.27	4.51	<0.001	3.41 (2.00–5.82)
TG18 grade					
I–II	—	—	—	—	1.00 (Reference)
III	1.39	0.28	5.01	<0.001	4.01 (2.33–6.89)
Surgery within 72 h					
No	—	—	—	—	1.00 (Reference)
Yes	−0.72	0.26	−2.77	0.006	0.49 (0.29–0.81)
Albumin (ALB)	−0.14	0.03	−3.92	<0.001	0.87 (0.82–0.93)
CRP	0.11	0.02	5.05	<0.001	1.12 (1.07–1.17)
Lymphocyte count (LY)	−1.12	0.23	−4.92	<0.001	0.32 (0.21–0.51)
CALLY index	−1.35	0.28	−4.81	<0.001	0.26 (0.15–0.45)

Abbreviations: S.E, standard error; OR, odds ratio; CI, confidence interval.

tribution may primarily reflect the sample composition of this cohort rather than a sex-specific effect.

Older age may reflect reduced physiological reserve and lower tolerance to surgical stress, which has been associated with worse postoperative outcomes after cholecystectomy [24]. Diabetes may increase postoperative vulnerability through impaired immune response, delayed tissue repair, and greater susceptibility to infection, and has also been reported as a factor associated with adverse outcomes after laparoscopic cholecystectomy [24]. Increased gallbladder wall thickness may indicate more severe local inflammation and greater operative difficulty, consistent with previous evidence linking gallbladder wall thickness >5 mm to complications after laparoscopic cholecystectomy [25]. Higher American Society of ASA-PS classification and the TG18 grade reflect greater systemic disease burden and more severe acute cholecystitis, respectively, and are clinically relevant in the TG18 surgical decision-making framework [5,24]. These factors may therefore help identify patients who require more careful preoperative assessment and postoperative monitoring.

AC is characterized by an inflammatory and immune response secondary to cystic duct obstruction, with pathological features including gallbladder wall edema, inflamma-

tory cell infiltration, microcirculatory disturbance, and local tissue necrosis [26]. The occurrence of postoperative complications is closely related to the patient's preoperative inflammatory status, immune function, and nutritional condition [27]. In the present study, a lower CALLY index was significantly associated with an increased risk of postoperative complications.

The CALLY index integrates CRP, albumin, and lymphocyte count. CRP is a classical acute-phase protein that reflects the severity of systemic inflammation. In AC, cystic duct obstruction and bacterial infection trigger the release of inflammatory mediators, leading to markedly elevated CRP levels. Persistent inflammation may impair gallbladder wall perfusion and promote tissue necrosis, while also increasing surgical difficulty, thereby predisposing patients to postoperative complications such as infection, abscess, and bleeding [7,28].

Albumin, an important indicator of nutritional status and hepatic synthetic function, reflects both metabolic reserve and inflammatory burden. Hypoalbuminemia may indicate malnutrition or systemic inflammatory consumption [29]. Reduced albumin levels can impair immune response, decrease tissue repair capacity, and lower colloid osmotic pressure, thereby increasing the risk of postopera-

Table 5. Multivariate logistic regression analysis of factors associated with postoperative complications.

Variable	β	S.E	Z	p value	OR (95% CI)
Age					
<60 years	—	—	—	—	1.00 (Reference)
60–70 years	1.22	0.41	2.99	0.003	3.39 (1.52–7.52)
>70 years	1.60	0.46	3.43	<0.001	4.93 (1.98–12.26)
Diabetes					
No	—	—	—	—	1.00 (Reference)
Yes	1.29	0.39	3.31	<0.001	3.64 (1.69–7.81)
Gallbladder wall thickness					
<5 mm	—	—	—	—	1.00 (Reference)
≥ 5 mm	1.13	0.34	3.30	<0.001	3.09 (1.58–6.05)
History of cholecystitis					
No	—	—	—	—	1.00 (Reference)
Yes	1.26	0.35	3.58	<0.001	3.52 (1.77–7.02)
ASA-PS classification					
I–II	—	—	—	—	1.00 (Reference)
III–IV	1.20	0.35	3.38	<0.001	3.31 (1.65–6.61)
TG18 grade					
I–II	—	—	—	—	1.00 (Reference)
III	1.43	0.36	3.99	<0.001	4.18 (2.07–8.43)
Surgery within 72 h					
No	—	—	—	—	1.00 (Reference)
Yes	–0.16	0.33	–0.49	0.627	0.85 (0.44–1.64)
CALLY index	–1.65	0.36	–4.58	<0.001	0.19 (0.10–0.39)

tive edema, infection, and poor wound healing [30,31,32].

Lymphocytes are key components of adaptive immunity, and decreased lymphocyte counts may indicate immunosuppression, which compromises the host's ability to eliminate pathogens and increases susceptibility to postoperative infections. In addition, recurrent episodes of cholecystitis may lead to pericholecystic adhesions and fibrosis, resulting in a distorted Calot's triangle and increased surgical complexity, thereby elevating the risk of intraoperative injury and postoperative complications [25,33].

In recent years, composite inflammation-based indices have gained increasing attention in surgical risk assessment. A previous study has shown that in patients undergoing colorectal cancer surgery, a lower preoperative CALLY index is significantly associated with a higher incidence of postoperative complications and worse perioperative outcomes [34]. Similarly, in gastric cancer, the preoperative CALLY index has been identified as an important predictor of overall survival and recurrence risk [35]. These findings suggest that the CALLY index, by incorporating markers of inflammation, immune status, and nutritional status, can comprehensively reflect patients' physiological reserve and may provide supplementary information for identifying patients at a higher risk of postoperative complications.

Despite growing evidence on inflammation-based composite indices, studies focusing on acute inflammatory conditions remain limited. Existing research on acute calculous cholecystitis has largely focused on the diagnostic value or

disease severity of single inflammatory or nutritional markers [36], rather than systematically evaluating their independent predictive value for postoperative complications. Moreover, most studies on composite indices in cardiovascular and critical care settings have primarily focused on overall prognosis or long-term outcomes [37], rather than specific perioperative complications. In addition, previous studies have often overlooked the specific associations between preoperative markers and different types of postoperative complications. To address these gaps, the present study systematically evaluated the predictive value of the CALLY index for postoperative complications in AC patients and, through multivariate analysis, provided preliminary evidence supporting the association between the CALLY index and postoperative complications in this clinical setting.

This study has several strengths. First, it systematically evaluated the predictive value of the CALLY index in AC patients undergoing cholecystectomy, expanding its application beyond oncological settings to acute inflammatory diseases. Second, a comprehensive set of clinical variables, including baseline characteristics, laboratory parameters, and perioperative factors, was included, and independent predictors were identified using multivariate logistic regression, thereby reducing potential confounding. Third, multiple statistical approaches, including correlation analysis and ROC curve analysis, were applied to assess the relationship between inflammatory markers and postoperative

complications from different perspectives, providing complementary perspectives on the observed associations.

However, several limitations should be acknowledged. First, this was a single-center retrospective study, which may be subject to selection bias, information bias, and residual confounding. Although multivariate logistic regression was performed to adjust for potential confounders, unmeasured or incompletely recorded variables could not be fully excluded. Second, the sample size was relatively limited, particularly for specific complication subtypes, which may affect the stability of complication-specific analyses. Third, all laboratory indicators were derived from a single preoperative measurement, although inflammatory and nutritional markers may fluctuate dynamically during disease progression and perioperative treatment. Finally, no formal model validation, calibration analysis, or decision curve analysis was performed in this study. Future multicenter prospective studies with larger sample sizes and formal external validation are needed to confirm the clinical utility and generalizability of the CALLY index in this setting.

Conclusions

This study demonstrated that a lower preoperative CALLY index was significantly associated with postoperative complications in patients with acute cholecystitis undergoing cholecystectomy. In addition, age, diabetes, gallbladder wall thickness, previous episodes of cholecystitis, ASA-PS classification, and TG18 grade were also associated with complication risk. These findings suggest that the CALLY index may provide supplementary information when evaluating patients before surgery. Further prospective multicenter studies with formal model validation are needed before this index can be applied as a clinical risk assessment tool.

Availability of Data and Materials

The data and materials in the current study are available from the corresponding author on reasonable request.

Author Contributions

HHC contributed to the study design. HHC and XYZ acquired and analyzed the data. YFY conducted the literature search and contributed to the interpretation of the data and results. All authors wrote the article. HHC contributed to the critical revision of the manuscript for important intellectual content. All authors read and approved the final manuscript. All authors have participated sufficiently in the work and agreed to be accountable for all aspects of the work.

Ethics Approval and Consent to Participate

This study was conducted in accordance with the Declaration of Helsinki and approved by the Medical Ethics Committee of Sir Run Run Shaw Hospital (Approval No.: 2026-

0369). As a retrospective study, all data were anonymized and extracted from electronic medical records, and the requirement for informed consent was waived by the ethics committee.

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Conflict of Interest

The authors declare no conflict of interest.

References

- [1] Gallaher JR, Charles A. Acute Cholecystitis: A Review. *JAMA*. 2022; 327: 965–975. <https://doi.org/10.1001/jama.2022.2350>
- [2] Tian J, Lu L, Tian S, Liu Y, Hu X, Wang Y, et al. Global, Regional, National Burden of Gallbladder and Biliary Diseases From 1990 to 2021 and Forecasted Trends by 2040. *Liver International : Official Journal of the International Association for the Study of the Liver*. 2025; 45: e70103. <https://doi.org/10.1111/liv.70103>
- [3] Dai F, Cai Y, Yang S, Zhang J, Dai Y. Global burden of gallbladder and biliary diseases (1990-2021) with healthcare workforce analysis and projections to 2035. *BMC Gastroenterology*. 2025; 25: 249. <https://doi.org/10.1186/s12876-025-03842-x>
- [4] Fugazzola P, Podda M, Tian BW, Cobianchi L, Ansaloni L, Catena F. Clinical update on acute cholecystitis and biliary pancreatitis: between certainties and grey areas. *EClinicalMedicine*. 2024; 77: 102880. <https://doi.org/10.1016/j.eclinm.2024.102880>
- [5] Okamoto K, Suzuki K, Takada T, Strasberg SM, Asbun HJ, Endo I, et al. Tokyo Guidelines 2018: flowchart for the management of acute cholecystitis. *Journal of Hepato-biliary-pancreatic Sciences*. 2018; 25: 55–72. <https://doi.org/10.1002/jhbp.516>
- [6] Pisano M, Allievi N, Gurusamy K, Borzellino G, Cimbanassi S, Boerna D, et al. 2020 World Society of Emergency Surgery updated guidelines for the diagnosis and treatment of acute calculus cholecystitis. *World Journal of Emergency Surgery : WJES*. 2020; 15: 61. <https://doi.org/10.1186/s13017-020-00336-x>
- [7] Kadirvel D, Vasudevan S, Selvamuthukumar S, Rajput S, Kumar PG. Identifying the Prognostic Factors Affecting the Conversion From Laparoscopic Cholecystectomy to Open Cholecystectomy in Acute Cholecystitis. *Cureus*. 2024; 16: e73975. <https://doi.org/10.7759/cureus.73975>
- [8] Wu H, Ma K, Liao B, Ji T, Zheng Z, Yan Y, et al. Multicenter external validation of a nomogram predicting conversion to open cholecystectomy during laparoscopic surgery for acute calculous cholecystitis: a cross-sectional study. *Scientific Reports*. 2025; 15: 18481. <https://doi.org/10.1038/s41598-025-03687-0>
- [9] Lalisang ANL, Wijaya DN, Jamtani I, Marbun VMG, Sihardo L, Ibrahim F, et al. Anticipating critical view of safety challenges in laparoscopic cholecystectomy for symptomatic cholelithiasis patients: Can we predict them earlier? *Turkish Journal of Surgery*. 2025; 41: 270–276. <https://doi.org/10.47717/turksurg.2025.6505>
- [10] Elkasaby MH, Elsayed H, Charo DC, Rashed MA, Elkoumi O, Elhaddad IM, et al. Antibiotic prophylaxis in emergency cholecystectomy for mild to moderate acute cholecystitis: a systematic review and meta-analysis of randomized controlled trials. *Perioperative Medicine (London, England)*. 2024; 13: 87. <https://doi.org/10.1186/s13741-024-00441-4>
- [11] Pesce A, Fabbri N, Bonazza L, Feo C. The role of fluorescent cholangiography to improve operative safety in different severity degrees

- of acute cholecystitis during emergency laparoscopic cholecystectomy: a prospective cohort study. *International Journal of Surgery* (London, England). 2024; 110: 7775–7781. <https://doi.org/10.1097/JS9.0000000000002160>
- [12] Chen Y, Kuo N, Lin HA, Chao CC, Lee S, Tsai CH, et al. Clinical and Imaging Characteristics to Discriminate Between Complicated and Uncomplicated Acute Cholecystitis: A Regression Model and Decision Tree Analysis. *Diagnostics* (Basel, Switzerland). 2025; 15: 1777. <https://doi.org/10.3390/diagnostics15141777>
 - [13] Erdoğan E, Naycı AE, Sevinc MM, Kınacı E, Orhan B, Idiz UO. How do inflammatory marker dynamics shift with acute calculous cholecystitis severity? *Ulusal Travma Ve Acil Cerrahi Dergisi = Turkish Journal of Trauma & Emergency Surgery : TJTES*. 2025; 31: 52–58. <https://doi.org/10.14744/tjtes.2024.08309>
 - [14] Turan OF, Sarcan E, Gedikasan S, Soylu A, Aksoy FM, Dodurga A, et al. Management of acute calculous cholecystitis in the emergency department: Evaluating the role of laboratory and radiological findings in a retrospective study. *Ulusal Travma Ve Acil Cerrahi Dergisi = Turkish Journal of Trauma & Emergency Surgery : TJTES*. 2025; 31: 161–166. <https://doi.org/10.14744/tjtes.2025.62703>
 - [15] Abdic A, Becirovic M, Becirovic E, Pasic F, Mehmedovic Z, Hadžić S, et al. C-reactive Protein and Biliary Complications as Independent Predictors of Hospital Stay in Acute Cholecystitis. *Cureus*. 2025; 17: e87598. <https://doi.org/10.7759/cureus.87598>
 - [16] Chen Y, Chen W. Association between malnutrition status and total joint arthroplasty periprosthetic joint infection and surgical site infection: a systematic review meta-analysis. *Journal of Orthopaedic Surgery and Research*. 2024; 19: 660. <https://doi.org/10.1186/s13018-024-05165-1>
 - [17] Orellana-Jaen A, Corres P, Orellana-Jaén J, Fernández-Escabias M, Carrilho-Candeias S, López-Cánovas JL, et al. Effects of Preoperative Immunonutrition on Postoperative Complications in Patients Undergoing Colorectal Cancer Resection: A Systematic Review and Meta-analysis. *Nutrition Reviews*. 2025; nuaf276. <https://doi.org/10.1093/nutrit/nuaf276>
 - [18] Wu B, Liu J, Shao C, Yu D, Liao J. Integrating inflammation, nutrition, and immunity: the CALLY index as a prognostic tool in digestive system cancers - a systematic review and meta-analysis. *BMC Cancer*. 2025; 25: 672. <https://doi.org/10.1186/s12885-025-14074-3>
 - [19] Shiraishi T, Nonaka T, Tominaga T, Takamura Y, Oishi K, Hashimoto S, et al. The C-reactive protein-albumin-lymphocyte (CALLY) index is a useful predictor of postoperative complications in patients with a colonic stent for obstructive colorectal cancer: a Japanese multicenter study. *Surgery Today*. 2025; 55: 502–509. <https://doi.org/10.1007/s00595-024-02924-9>
 - [20] Fukushima N, Masuda T, Tsuboi K, Takahashi K, Yuda M, Fujisaki M, et al. Prognostic significance of the preoperative C-reactive protein-albumin-lymphocyte (CALLY) index on outcomes after gastrectomy for gastric cancer. *Surgery Today*. 2024; 54: 943–952. <https://doi.org/10.1007/s00595-024-02813-1>
 - [21] Zhao H, Yin B, Li XR, Liu XY, Bu ZT, Shi HP. The CRP-albumin-lymphocyte index provides enhanced prognostic value in liver cancer compared to the TNM staging system. *Scientific Reports*. 2025; 15: 20090. <https://doi.org/10.1038/s41598-025-03985-7>
 - [22] Saetang M, Kunapaisal T, Wasinwong W, Boonthum P, Sriyanaluk B, Nuanjun K. Predictors associated with Clavien-Dindo complications in lung cancer surgery: A retrospective cohort study. *PloS One*. 2024; 19: e0316214. <https://doi.org/10.1371/journal.pone.0316214>
 - [23] Farahani PK, Nejat SK. Preoperative C-reactive protein as a predictor of conversion and complications in laparoscopic cholecystectomy for acute cholecystitis. *BMC Surgery*. 2025; 25: 476. <https://doi.org/10.1186/s12893-025-03212-0>
 - [24] Lee H, Han IW, Choi JE, Lee HK. Surgical risk calculator development for postoperative outcomes after laparoscopic cholecystectomy: a multicenter prospective cohort study. *Annals of Surgical Treatment and Research*. 2025; 108: 352–361. <https://doi.org/10.4174/ast.2025.108.6.352>
 - [25] Fu JN, Liu SC, Chen Y, Zhao J, Ma T. Analysis of risk factors for complications after laparoscopic cholecystectomy. *Heliyon*. 2023; 9: e18883. <https://doi.org/10.1016/j.heliyon.2023.e18883>
 - [26] Adachi T, Eguchi S, Muto Y. Pathophysiology and pathology of acute cholecystitis: A secondary publication of the Japanese version from 1992. *Journal of Hepato-biliary-pancreatic Sciences*. 2022; 29: 212–216. <https://doi.org/10.1002/jhbp.912>
 - [27] Heutlinger O, Acharya N, Tedesco A, Ramesh A, Smith B, Nguyen NT, et al. Nutritional Optimization of the Surgical Patient: A Narrative Review. *Advances in Nutrition* (Bethesda, Md.). 2025; 16: 100351. <https://doi.org/10.1016/j.advnut.2024.100351>
 - [28] Mencarini L, Vestito A, Zagari RM, Montagnani M. The Diagnosis and Treatment of Acute Cholecystitis: A Comprehensive Narrative Review for a Practical Approach. *Journal of Clinical Medicine*. 2024; 13: 2695. <https://doi.org/10.3390/jcm13092695>
 - [29] Li Y, Chen L, Yang X, Cui H, Li Z, Chen W, et al. Dynamic association of serum albumin changes with inflammation, nutritional status and clinical outcomes: a secondary analysis of a large prospective observational cohort study. *European Journal of Medical Research*. 2025; 30: 679. <https://doi.org/10.1186/s40001-025-02925-5>
 - [30] Aldecoa C, Llaui JV, Nuvials X, Artigas A. Role of albumin in the preservation of endothelial glycocalyx integrity and the microcirculation: a review. *Annals of Intensive Care*. 2020; 10: 85. <https://doi.org/10.1186/s13613-020-00697-1>
 - [31] Wiedermann CJ. Hypoalbuminemia as Surrogate and Culprit of Infections. *International Journal of Molecular Sciences*. 2021; 22: 4496. <https://doi.org/10.3390/ijms22094496>
 - [32] Nipper CA, Lim K, Riveros C, Hsu E, Ranganathan S, Xu J, et al. The Association between Serum Albumin and Post-Operative Outcomes among Patients Undergoing Common Surgical Procedures: An Analysis of a Multi-Specialty Surgical Cohort from the National Surgical Quality Improvement Program (NSQIP). *Journal of Clinical Medicine*. 2022; 11: 6543. <https://doi.org/10.3390/jcm11216543>
 - [33] Jindal A, Badu NYA, Katiki C, Ponnappalli VJS, Desai KJ, Mansoor S, et al. Factors Influencing Bile Duct Injuries: A Dreaded Complication of Laparoscopic Cholecystectomy. *Cureus*. 2024; 16: e73600. <https://doi.org/10.7759/cureus.73600>
 - [34] Takeda Y, Sugano H, Okamoto A, Nakano T, Shimoyama Y, Takada N, et al. Prognostic usefulness of the C-reactive protein-albumin-lymphocyte (CALLY) index as a novel biomarker in patients undergoing colorectal cancer surgery. *Asian Journal of Surgery*. 2024; 47: 3492–3498. <https://doi.org/10.1016/j.asjsur.2024.03.054>
 - [35] Li J, Zhang S, Hu X, Huang T, Chen M. Correlation between the C-reactive protein (CRP)-albumin-lymphocyte (CALLY) index and the prognosis of gastric cancer patients after gastrectomy: a systematic review and meta-analysis. *Surgery Today*. 2025; 55: 483–491. <https://doi.org/10.1007/s00595-024-02921-y>
 - [36] He B, He Q, Lai Z, Niu Z, Zhang J, Wang Y. The Value of Systemic Inflammatory Index and Nutritional Marker in Predicting Acute Calculous Cholecystitis and Its Severity. *Journal of Inflammation Research*. 2025; 18: 9505–9521. <https://doi.org/10.2147/JIR.S521080>
 - [37] Arin CB, Dahir OF, Adan AS, Abdi IA, Karataş M. Systemic inflammatory indices and mortality risk in heart failure: a retrospective cohort study. *Frontiers in Cardiovascular Medicine*. 2025; 12: 1626470. <https://doi.org/10.3389/fcvm.2025.1626470>

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