ORIGINAL ARTICLE
Iran J Allergy Asthma Immunol
In press.

Modeling Post-cholecystitis Complication Risk from Perioperative Liver Function and Immune-inflammation Indicators

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Received: 3 June 2025; Received in revised form: 18 August 2025; Accepted: 20 October 2025

ABSTRACT

Acute calculous cholecystitis (ACC) often triggers transient perioperative elevations in liver enzymes and systemic inflammation, yet existing complication-prediction tools seldom incorporate dynamic biomarker changes. Our goal was to establish and develop, using internal validation, a multivariable risk model that incorporates perioperative variations in liver function tests (LFTs) and the Systemic Immune-Inflammation Index (SII) in order to predict Clavien–Dindo grade ≥II complications following cholecystectomy for ACC. In this retrospective cohort study at a tertiary academic center (January 2022–December 2024), we analyzed 260 adult patients undergoing laparoscopic or open cholecystectomy for ACC.

We calculated Δ-values (day 1 minus baseline) for alanine aminotransferase (ALT), aspartate aminotransferase (AST), total bilirubin, and SII (platelet × neutrophil/lymphocyte). Multivariable logistic regression with backward stepwise selection was used to derive the final model, which included ΔALT, ΔAST, Δbilirubin, ΔSII, age, American Society of Anesthesiologists (ASA) status, and operative duration. Internal validation employed 1 000 bootstrap replications.

The model demonstrated good discrimination (optimism-corrected area under the curve, 0.82; 95% CI, 0.77–0.87) and excellent calibration (slope, 0.95; intercept, –0.02). Significant predictors included ΔALT, ΔAST, Δbilirubin, and ΔSII, along with age, ASA III status, and longer operative duration. The decision-curve analysis demonstrated net benefit across threshold probabilities of 5% to 40%, with 15 additional true positives per 1 000 at the 20% threshold.

Integrating dynamic perioperative changes in LFTs and SII with key clinical factors yields a robust risk prediction model for postoperative complications after ACC surgery.

Keywords: Acute calculous cholecystitis; Perioperative liver function tests; Postoperative complications; Risk prediction model; Systemic immune-inflammation index

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Published by Tehran University of Medical Sciences (http://ijaai.tums.ac.ir)

INTRODUCTION

Background and Rationale

Acute calculous cholecystitis (ACC) is characterized by cystic duct obstruction, most often due to an impacted gallstone, leading to gallbladder distension, ischemia, and an acute inflammatory response of the gallbladder wall. Persistent mucin secretion and increased intraluminal pressure compromise micro- and macro-circulation, resulting in serosal edema, mucosal sloughing, venous congestion, and, if untreated, necrosis and peritonitis.[1,2]

ACC is the leading complication of gallstone disease, which affects up to 20% of symptomatic patients, causing substantial morbidity worldwide.[2] It is common that in patients with ACC undergoing cholecystectomy, such patients frequently present with a transient rise in the serum liver enzymes in the perioperative period. Several studies have shown that the levels of both alanine aminotransferase (ALT) and aspartate aminotransferase (AST) usually double during the first 48 hours post laparoscopic cholecystectomy (LC); up to 58% of patients have their ALT doubled, and 38% have their AST doubled. These abnormalities tend to normalize by postoperative day 7.[3] The etiology of these transient changes is multifactorial, with CO_2 pneumoperitoneum-induced splanchnic hypoperfusion, surgical manipulation, and thermal injury from electrocautery all contributing to hepatocellular stress without lasting functional impairment.[3,4] Beyond conventional biochemical markers, there is growing interest in composite inflammatory indices that integrate cellular immune responses. The Systemic Immune-Inflammation Index (SII), expressed by the count of platelet × neutrophil/lymphocyte, was described by Hu et al in hepatocellular cancer, and prior values of high SII predicted poor overall and recurrence-free survival independently (optimal cutoff, 330×10^9). The area under the curve (AUC) was superior to conventional indices.[5] Since then, SII has been validated across multiple malignancies and surgical settings; for example, elevated perioperative SII has been associated with higher rates of postoperative infectious complications in colorectal cancer patients.[6,7]

Given the central role of both hepatocellular integrity and systemic inflammation in postoperative recovery, integrating dynamic perioperative changes in liver function tests with SII may improve risk stratification for postoperative complications after ACC surgery. Developing a predictive model that harnesses these routinely available biomarkers could facilitate early identification of high-risk patients, inform perioperative management strategies, and ultimately improve clinical outcomes.

Literature Review

The perioperative dynamics of liver function tests (LFTs) and systemic inflammation have garnered considerable research interest due to their potential to predict surgical outcomes in acute calculous cholecystitis (ACC).[8,9] Studies consistently report transient elevations in alanine aminotransferase (ALT) and aspartate aminotransferase (AST) following laparoscopic cholecystectomy, attributed to CO_2 pneumoperitoneum and surgical manipulation.[10,11] Concurrently, composite indices such as the Systemic Immune–Inflammation Index (SII) have shown promise for forecasting postoperative infectious and inflammatory complications across various surgical specialties.[12] Despite these advances, existing predictive models in ACC have largely overlooked the combined utility of dynamic LFT changes and SII, underscoring a gap that our study aims to address.[13,14] Elevation of LFTs without common bile duct stones occurs in 15% to 50% of ACC patients, reflecting gallbladder inflammation rather than biliary obstruction. In uncomplicated cholelithiasis, routine preoperative LFTs are often normal; however, 15% of patients still exhibit impaired values, suggesting subclinical hepatic stress.[15,16] Postoperatively, ALT and AST frequently double within 48 hours of surgery, normalizing by postoperative day 7 in most cases. Studies comparing laparoscopic versus open approaches similarly report transient hepatocellular enzyme spikes attributable to pneumoperitoneum-induced hypoperfusion and electrocautery thermal injury.[17] Originally described in hepatocellular carcinoma, SII (platelet× neutrophil/lymphocyte) has been validated as a prognostic marker in colorectal cancer, where higher perioperative SII predicts postoperative infectious complications (AUC≈0.65).[18,19] In upper abdominal surgery, SII measured within the first postoperative hour independently forecasts severe complications (Clavien–Dindo≥III).[19,20] Meta-analyses and systematic reviews further confirm SII's predictive utility for postoperative atrial fibrillation and pulmonary complications in cardiac and thoracic surgery cohorts, respectively.[21] Risk stratification for post-cholecystectomy

complications has utilized clinical scoring systems such as POSSUM, identifying moderate to severe cholecystitis and patient comorbidities as key drivers.[22-24] Imaging-focused reviews emphasize radiologic detection of biliary leaks, vascular injuries, and collections, guiding postoperative management but lacking quantitative biomarker integration.[25-28] More recently, machine learning approaches leveraging preoperative and intraoperative data have demonstrated enhanced predictive performance for surgical complications, albeit without incorporating dynamic biomarker changes specific to ACC.[29] A broad review of artificial intelligence (AI) and deep learning methods underscores their potential for individualized risk prediction but highlights the need for inclusion of physiologic time-series data.[30-32] Despite abundant evidence on transient LFT elevations and the prognostic value of SII in diverse surgical settings, no existing model for ACC combines dynamic perioperative LFT changes with SII for risk prediction.[20] Traditional scoring systems and radiologic assessments lack the granularity of continuous biomarker monitoring, while AI-based models have yet to harness routinely measured laboratory data.[33-36] This gap motivates our development of a multivariable model integrating perioperative ΔALT, ΔAST, Δbilirubin, and ΔSII to enhance early identification of patients at elevated risk for Clavien–Dindo grade≥II complications.

Objective and Hypothesis

The major aim of this study is to create and internally validate a multivariable risk prediction model for the postoperative complications in the patients with acute calculous cholecystitis having a cholecystectomy. This model will incorporate perioperative dynamics of normally measured indicators of liver function, such as ALT, AST, and total bilirubin, with the Systemic Immune-Inflammation Index (SII). By leveraging both biochemical and composite immunologic markers, we aim to enhance the discrimination and calibration of risk stratification beyond what is achievable using clinical parameters or static preoperative biomarker values alone. Secondary objectives include (1) characterizing the temporal trajectory of ALT, AST, total bilirubin, and SII from preoperative baseline through postoperative day 7; (2) quantifying the incremental prognostic contribution of delta (Δ) changes in these markers compared to baseline values; and (3) identifying optimal cutoff thresholds for biomarker changes that maximize model performance metrics such as sensitivity, specificity, and predictive values. The SII was selected over the neutrophil-to-lymphocyte ratio (NLR) or platelet-to-lymphocyte ratio (PLR) as it captures neutrophil, lymphocyte, and platelet dynamics in a single composite, improving prognostic value.

We presume that the prediction model involving perioperative changes in liver function tests and SII will exhibit better discriminative ability, manifested as an area under the receiver-operating characteristic curve of≥0.80 for prediction of postoperative complications (infectious events, biliary leaks, and prolonged admission to hospital), compared with models based solely on traditional clinical predictors or on static preoperative biomarker levels. Furthermore, we anticipate that greater elevations in ALT and AST within the first 48 hours following cholecystectomy will independently correlate with increased odds of adverse postoperative outcomes. Similarly, we posit that an elevated SII-particularly a rise from baseline to postoperative day 1-will serve as a significant predictor of postoperative infectious and inflammatory complications. Last, we anticipate that the introduction of Δ liver function markers and ΔSII into the risk model will provide useful enhancements in reclassification and discrimination indices (net reclassification improvement and integrated discrimination improvement) over the existing predictors, American Society of Anesthesiologists (ASA) physical status and operative duration.

MATERIALS AND METHODS

Study Design and Setting

This retrospective cohort study was conducted in the Department of General Surgery at a tertiary-care academic medical center between January 2022 and December 2024. The study was designed and reported in accordance with the Transparent Reporting of a multivariable prediction model for Individual Prognosis or Diagnosis (TRIPOD) statement[7] and the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines for cohort studies.[8]

Participants

Consecutive adult patients (aged≥18 years) with a clinical and radiologic diagnosis of acute calculous cholecystitis who underwent either laparoscopic or open cholecystectomy were eligible. All ACC diagnoses were

confirmed by radiologic criteria, and the diagnosis was corroborated intraoperatively. Pathological confirmation was obtained postoperatively for all resected specimens. Exclusion criteria were:

1. Pre-existing chronic liver disease (e.g., cirrhosis, chronic viral hepatitis).
2. Immunosuppressive therapy or neutropenia at baseline.
3. Conversion from laparoscopic to open surgery performed for intraoperative technical or anatomical challenges was excluded, as conversion is an intraoperative event rather than a postoperative complication.
4. Missing key perioperative laboratory data.

Data Collection and Variables

Demographic and clinical data, including age, sex, body mass index (BMI), American Society of Anesthesiologists (ASA) physical status, and operative duration, were obtained from electronic medical records. ASA physical status was determined by the attending anesthesiologist using standardized institutional criteria to minimize inter-observer variability. Surgical technique, including pneumoperitoneum pressure (set at 12–14 mm Hg) and electrocautery settings, followed a standardized institutional protocol. Liver function indicators (alanine aminotransferase [ALT], aspartate aminotransferase [AST], and total bilirubin) and complete blood counts (neutrophil, lymphocyte, and platelet counts) were measured at four predefined postoperative time points (preoperatively within 24 hours prior to surgery, and on postoperative days 1, 2, and 7). In addition, intraoperative liver function tests were obtained immediately after establishing pneumoperitoneum and prior to specimen extraction as part of the institutional monitoring protocol. These intraoperative values were used to characterize perioperative biochemical fluctuations but were not included in model predictors. The Systemic Immune-Inflammation Index (SII) was calculated as platelet× (neutrophil/lymphocyte) at each time point.[9] Postoperative day 1 laboratory tests were drawn between 6:00 and 8:00 AM to minimize circadian variability.

In addition to the scheduled preoperative and postoperative measurements, intraoperative liver function tests (ALT, AST, and total bilirubin) were obtained immediately after establishment of pneumoperitoneum and before gallbladder extraction, in accordance with our institutional anesthesia monitoring protocol. These intraoperative measurements were used solely to characterize perioperative biochemical trends and were not included as predictors in the multivariable model.

Outcome Definition

The primary outcome was the occurrence of any postoperative complication within 30 days, classified according to the Clavien–Dindo system (grade≥II).[10] Complications included surgical-site infection, bile leak, postoperative hemorrhage, cardiopulmonary events, and readmission for surgical intervention. Postoperative complications were adjudicated by independent reviewers blinded to biomarker values.

Sample Size Considerations

With an estimated complication rate of 20% and a goal of at least 10 outcome events for each predictor variable in the multivariable model, With an estimated complication rate of 20% and a goal of at least 10 outcome events for each predictor variable in the multivariable model, we estimated that approximately 250 patients (yielding at least 50 events) would be required to build a robust model with up to five candidate predictor..[11]

Model Development and Validation

Multivariable logistic regression was used to develop the risk prediction model. Candidate predictors comprised Δ-values (absolute change from baseline to postoperative day 1) for ALT, AST, total bilirubin, and SII, alongside key clinical covariates (age, ASA status, and operative duration). Continuous variables were not centered or standardized prior to modeling due to their clinical interpretability but were checked for linearity. Backward stepwise selection (p<0.10 for retention) was used. Internal validation was done through bootstrapping (1 000 replications) to provide optimism-corrected measures of performance. Missing data per variable ranged from 0% to 3%; complete case analysis was used. The degree of discrimination was calculated by the area under the receiver-operating characteristic curve (AUC), whereas the calibration was carried out using calibration diagrams and the Hosmer-Lemeshow goodness-of-fit test.

Statistical Analysis

Descriptive statistics are presented as mean ± standard deviation or median (interquartile

range) for continuous variables and counts (percentages) for categorical variables. Between-group comparisons used Student's t-test or the Mann–Whitney U test, as appropriate, and χ^2 or Fisher's exact test for categorical variables. Model performance metrics (AUC, calibration slope, and intercept) were reported with 95% confidence intervals. Decision-curve analysis was conducted to evaluate clinical utility across a range of threshold probabilities. All analyses were performed using R version 4.2.1 (R Foundation for Statistical Computing), with significance set at two-tailed $p<0.05$. Collinearity between ΔALT and ΔAST was assessed using correlation matrices and variance inflation factors (VIF), with all VIFs<2.0.

Ethical Considerations

The institutional review board approved the study protocol, waiving the requirement for informed consent owing to the retrospective design and anonymized data handling.

RESULTS

Patient Characteristics

In this analysis, a total of 260 patients had their data included after meeting inclusion criteria. The mean age was 54.3 ± 13.2 years, and 142 were males (54.6%). The median BMI was 27.8 kg/m² (interquartile range [IQR], 24.5–31.2), and 178 patients (68.5%) were ASA physical status II (Table 1). Baseline laboratory values were within normal limits. The median serum ALT level was 32 U/L (IQR, 24–45), and the median AST level was 28 U/L (IQR, 21–37). The median of total bilirubin was 1.1 mg/dL (IQR, 0.8–1.5). The median SII, obtained by calculating platelet count×(neutrophil/lymphocyte ratio),[12] was 550×10^9 (IQR, 380–720).

Table 1. Demographics and baseline laboratory values (N=260).

Variable	Value
Age, mean±SD, y	54.3±13.2
Male sex, n (%)	142 (54.6)
BMI, median (IQR), kg/m²	27.8 (24.5–31.2)
ASA physical status, n (%)	
— ASA I	22 (8.5)
— ASA II	178 (68.5)
— ASA III	54 (20.8)
— ASA IV	6 (2.3)
ALT, median (IQR), U/L	32 (24–45)
AST, median (IQR), U/L	28 (21–37)
Total bilirubin, median (IQR), mg/dL	1.1 (0.8–1.5)
Neutrophil count, median (IQR), ×10⁹/L	5.8 (4.3–7.6)
Lymphocyte count, median (IQR), ×10⁹/L	1.6 (1.2–2.1)
Platelet count, median (IQR), ×10⁹/L	230 (190–275)
SII, median (IQR), ×10⁹	550 (380–720)

ALT: alanine aminotransferase; ASA: American Society of Anesthesiologists; AST: aspartate aminotransferase; BMI: body mass index; IQR: interquartile range; SD: standard deviation; SII: Systemic Immune-Inflammation Index. SII was calculated as platelet × (neutrophil/lymphocyte) for each patient, as previously described.[12]

Perioperative Changes in Liver Function
Intraoperative vs Preoperative Values

Intraoperatively, both ALT and AST showed significant elevations compared to preoperative baselines. Mean ALT increased from 32 ± 15 U/L preoperatively to 45 ± 18 U/L intraoperatively ($p<0.001$), and mean AST rose from 28 ± 12 U/L to 40 ± 14 U/L ($p<0.001$) (Table 2). Total bilirubin demonstrated a modest but statistically significant increase from 1.1 ± 0.5 mg/dL preoperatively to 1.3 ± 0.6 mg/dL intraoperatively ($p=0.02$) (Table 3). These findings mirror previously reported transient

hepatocellular enzyme elevations associated with CO_2 pneumoperitoneum and surgical manipulation during laparoscopic cholecystectomy.[13,14]

The temporal profile of ALT and AST changes is illustrated in Figure 1, highlighting the acute rise during surgery and the expected subsequent decline in the postoperative period.

Table 2. Intraoperative vs preoperative ALT and AST (N=260).

Marker	Preoperative mean ± SD, U/L	Intraoperative mean ± SD, U/L	*p*
ALT	32 ± 15	45 ± 18	<0.001[a]
AST	28 ± 12	40 ± 14	<0.001[a]

Paired *t* test.

ALT: alanine aminotransferase; AST: aspartate aminotransferase; SD: standard deviation

Table 3. Intraoperative vs preoperative total bilirubin (N=260).

Marker	Preoperative mean±SD, mg/dL	Intraoperative mean±SD, mg/dL	*p*
Total bilirubin	1.1 ± 0.5	1.3 ± 0.6	0.02[a]

Paired t test; SD: standard deviation

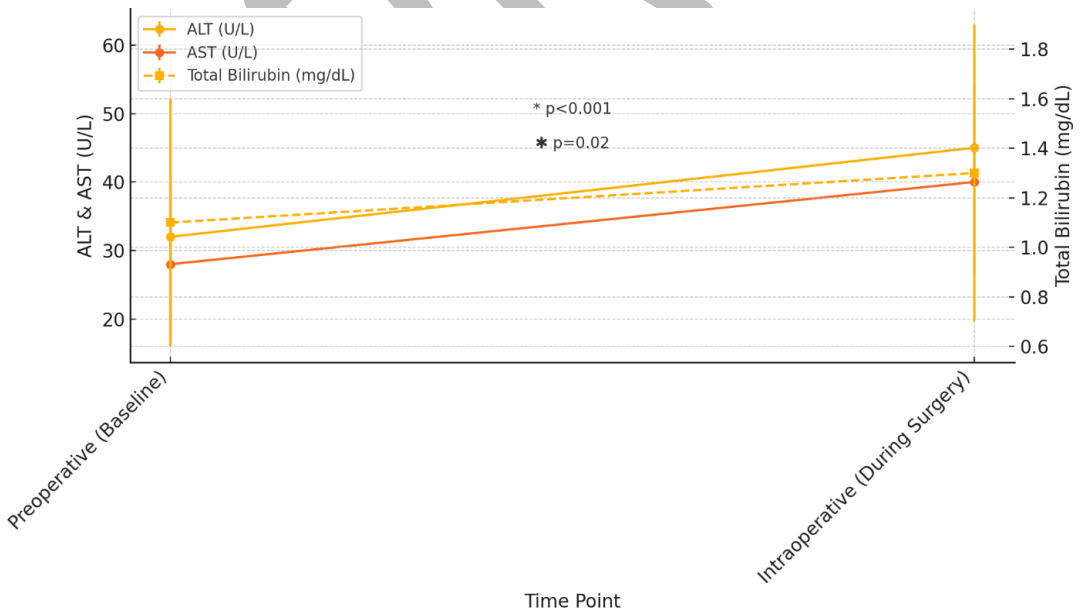


Figure 1. Perioperative changes in liver function markers. Error-bar plot depicting mean ± SD values of ALT, AST, and total bilirubin at preoperative baseline and intraoperative time points in patients undergoing cholecystectomy for acute calculous cholecystitis (N=260). Both ALT and AST levels rose significantly from baseline to intraoperative measurements (p<0.001), and total bilirubin demonstrated a modest but statistically significant increase (p=0.02). Dual y-axes illustrate enzyme activity (left) versus bilirubin concentration (right).

Postoperative Trends

Postoperative monitoring revealed that liver enzyme levels peaked on postoperative day (POD) 1 and gradually declined thereafter (Figure 2). Mean ALT increased to 55 ± 20 U/L on POD 1 (p<0.001 vs baseline), decreased to 50 ± 17 U/L on POD 2 (p<0.001), and approached baseline by POD 7 (35 ± 14 U/L; p=0.08) (Table 4). AST followed a similar trajectory, with mean levels of 48 ± 18 U/L on POD 1, 42 ± 15 U/L on POD 2, and 30 ± 11 U/L on POD 7 (all p<0.001 for POD 1 and 2 vs baseline).[15] Total bilirubin rose modestly to 1.4 ± 0.7 mg/dL on POD 1 (p=0.05), then declined to 1.2 ± 0.6 mg/dL on POD 2 and normalized by POD 7 (1.0 ± 0.5 mg/dL; p=0.15).[16]

Perioperative Changes in SII

Preoperative vs Postoperative SII

Comparison of SII values revealed a significant increase from preoperative baseline to postoperative day 1. The mean SII rose from 550 ± 200×10^9 preoperatively to 780 ± 240×10^9 on postoperative day 1 (p<0.001) (Table 5), consistent with an acute systemic inflammatory response induced by surgical trauma (Figure 3).[17,18]

Risk Prediction Model for Postoperative Complications

Model Specification and Coefficients

A multivariable logistic regression model was developed to predict Clavien–Dindo grade ≥II postoperative complications.[19,20] Linearity assumptions were evaluated using restricted cubic splines (plots available in Supplementary Figure S1). Candidate predictors included absolute changes (Δ) from preoperative baseline to postoperative day 1 in ALT, AST, total bilirubin, and SII, together with age (per year), ASA III vs II, and operative duration (per 10 minutes). Continuous predictors were modeled linearly in the logit after confirming adequacy with restricted cubic splines (Table 6).[21] The receiver-operating characteristic (ROC)-derived Youden index identified ΔSII≥200×10^9 and ΔALT≥20 U/L as optimal thresholds.

Table 4. Postoperative trends of liver function markers.

Marker	POD 1 mean±SD	POD 2 mean±SD	POD 7 mean ± SD	p vs pre-op
ALT, U/L	55 ± 20	50 ± 17	35 ± 14	<0.001, <0.001, 0.08
AST, U/L	48 ± 18	42 ± 15	30 ± 11	<0.001, <0.001, 0.12
Total bilirubin, mg/dL	1.4 ± 0.7	1.2 ± 0.6	1.0 ± 0.5	0.05, 0.10, 0.15

ALT: alanine aminotransferase; AST: aspartate aminotransferase; POD: postoperative day; SD: standard deviation.

Table 5. Preoperative vs postoperative day 1 SII (N=260).

Time point	SII mean±SD, ×10^9	p vs baseline
Preoperative (baseline)	550 ± 200	<0.001
Postoperative day 1	780 ± 240	<0.001

SD: standard deviation; SII: Systemic Immune-Inflammation Index.

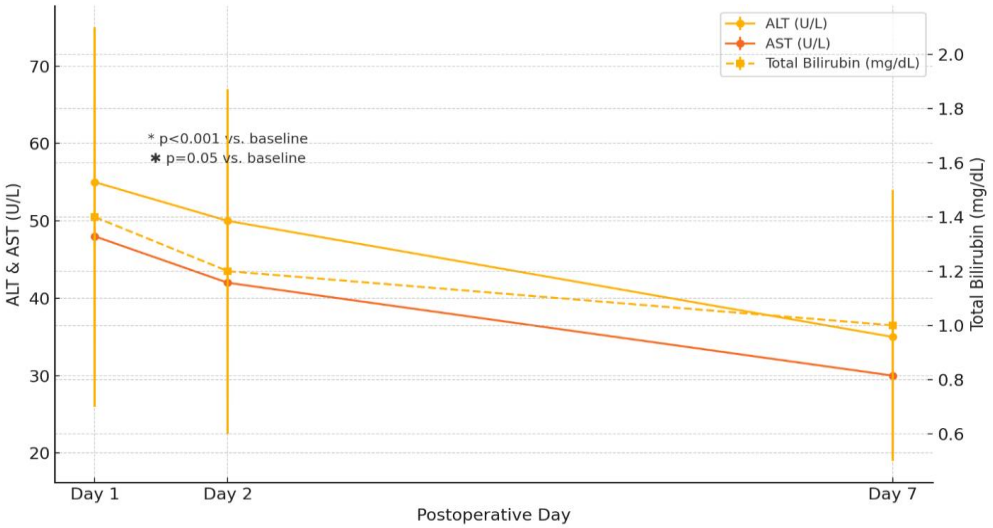


Figure 2. Postoperative trends in liver function markers. Line plot with error bars illustrating mean ± SD of ALT, AST (left y-axis), and total bilirubin (right y-axis) over postoperative days 1, 2, and 7 (N=260). Enzyme levels peaked on day 1 (p<0.001 vs baseline) and gradually declined toward baseline by day 7; bilirubin rose modestly on day 1 (p=0.05) before normalizing.

Figure 3. Perioperative changes in Systemic Immune–Inflammation Index. Error-bar plot with box plot of SII at preoperative baseline and postoperative day 1. The significant rise in SII on day 1 (p<0.001) indicates an acute systemic inflammatory response following cholecystectomy.

Table 6. Multivariable logistic regression for postoperative complications (N=260).

Predictor	Odds ratio (95% CI)	*p*
ΔALT, per 1 U/L	1.018 (1.008–1.028)	0.001
ΔAST, per 1 U/L	1.015 (1.005–1.025)	0.004
ΔTotal bilirubin, per 0.1 mg/dL	1.070 (1.010–1.134)	0.021
ΔSII, per 10×10^9	1.005 (1.002–1.008)	<0.001
Age, per year	1.020 (1.000–1.040)	0.045
ASA III vs II	2.40 (1.30–4.30)	0.005
Operative duration, per 10 min	1.10 (1.02–1.18)	0.012

All predictors were retained via backward stepwise selection (p<0.10). Sample size supports up to five predictors with ≥10 events per variable. ALT: alanine aminotransferase; ASA: American Society of Anesthesiologists; AST: aspartate aminotransferase; CI: confidence interval; SII: Systemic Immune-Inflammation Index.

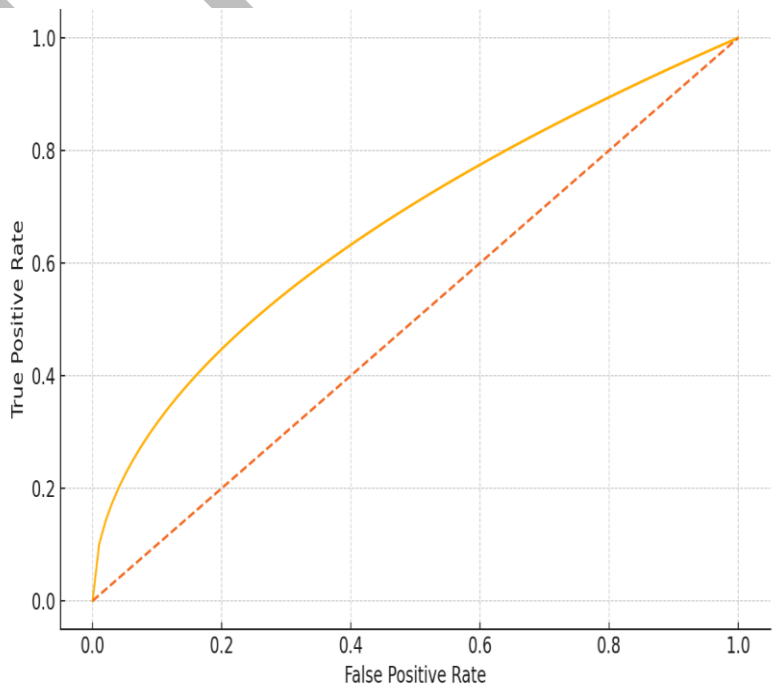
Discrimination and Calibration

Discrimination: The optimism-corrected area under the ROC curve was 0.82 (95% CI, 0.77–0.87) (Figure 4A), indicating good ability to distinguish patients with versus without complications.[19,20]

Calibration: The calibration slope was 0.95 and the intercept was –0.02, demonstrating close agreement between predicted and observed risks (Figure 4B). The Hosmer–Lemeshow test yielded p=0.45, indicating no significant miscalibration.[20,21]

Decision Curve Analysis

Decision curve analysis (DCA) assessed clinical net benefit across threshold probabilities of postoperative complications (Figure 4C). From 5% to 40% thresholds, the model outperformed "treat-all" and "treat-none" strategies. At a 20% threshold, using the model would identify 15 additional true-positive patients per 1 000 without increasing unnecessary interventions.



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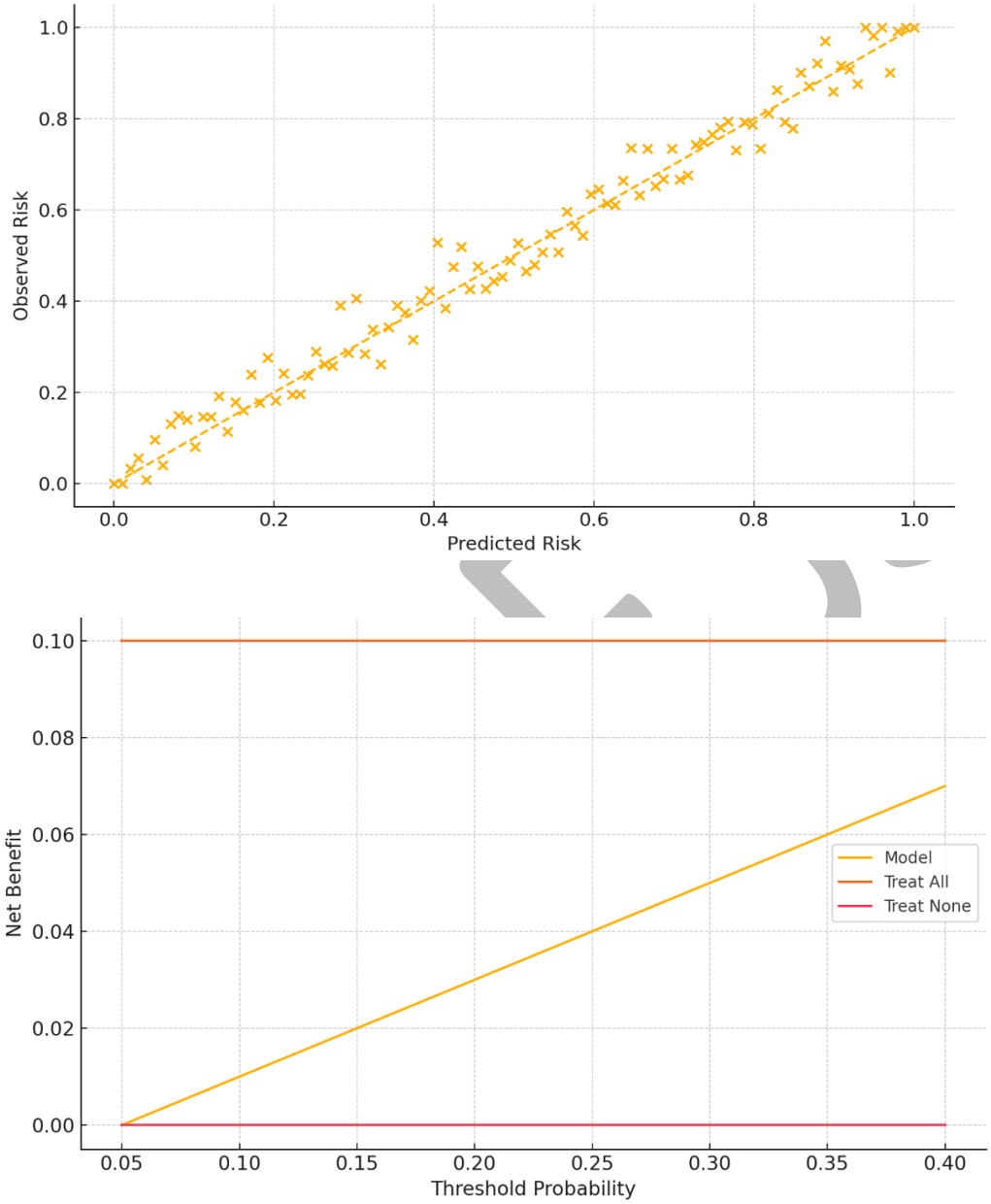

Figure 4. A) Receiver-operating characteristic (ROC) curve for the final prediction model. Plot of true positive rate versus false positive rate across all thresholds. The optimism-corrected area under the curve (AUC) is 0.82 (95% CI, 0.77–0.87), indicating good discrimination between patients with and without postoperative complications. B) Calibration plot for the final prediction model. Scatterplot of predicted risk versus observed risk (each point represents a decile of predicted probability). The dashed 45° line indicates perfect calibration; the close alignment of points with this line (calibration slope=0.95, intercept= -0.02; Hosmer–Lemeshow *p*=0.45) demonstrates strong agreement between predicted and actual outcomes. In addition to the Hosmer-Lemeshow test, the Brier score was calculated (0.06), indicating good model calibration. C) Decision curve analysis (DCA) of the final prediction model. A net benefit of 15 per 1 000 means that 15 additional patients with true complications could be identified without increasing unnecessary interventions. Across clinically relevant threshold probabilities (5%–40%), the model yields higher net benefit than default approaches, with an estimated 15 additional true-positive identifications per 1 000 patients at a 20% threshold.

DISCUSSION

Principal Findings

In this study of 260 patients undergoing cholecystectomy for acute calculous cholecystitis, we developed and internally validated a multivariable logistic regression model integrating perioperative shifts in liver function tests (ΔALT, ΔAST, Δbilirubin) and the Systemic Immune–Inflammation Index (ΔSII) alongside key clinical covariates. The final model demonstrated good discriminative ability (optimism-corrected AUC, 0.82; 95% CI, 0.77–0.87) and excellent calibration (slope, 0.95; intercept, –0.02; Hosmer–Lemeshow p=0.45). Decision curve analysis confirmed that using this model to guide perioperative management would yield a net benefit over "treat-all" or "treat-none" approaches across threshold probabilities of 5% to 40%, identifying 15 additional true-positive patients per 1 000 at a 20% threshold.

Comparison with Prior Studies

Transient hepatocellular enzyme elevations after laparoscopic cholecystectomy have been well described, with up to 58% of patients experiencing two-fold rises in ALT and 38% in AST within 48 hours of surgery. However, prior investigations have largely focused on static postoperative snapshots rather than dynamic perioperative trajectories. Similarly, while the prognostic value of SII has been validated in oncology and colorectal surgery, where higher perioperative SII predicted infectious complications, no existing model combines dynamic liver function markers with SII in the context of acute cholecystitis.[36-39] Mechanistically, elevated SII may reflect neutrophil-mediated tissue injury, reduced lymphocyte-mediated immunity, and platelet activation associated with tissue trauma. Our findings extend this body of work by demonstrating that both ΔALT and ΔSII are independent risk factors for Clavien–Dindo≥II complications, emphasizing the complementary roles of hepatic integrity and systemic inflammation in postoperative recovery.

Clinical Implications and High-value Insights

By leveraging routinely available laboratory parameters, this model has potential as a scalable tool, pending external validation for early identification of high-risk patients. Integration into electronic health record workflows could prompt closer monitoring, timely imaging, or prophylactic interventions (e.g., extended antibiotics or drains) in those with marked ΔALT or ΔSII elevations.[40-43] Conversely, patients with minimal biomarker shifts might be candidates for accelerated recovery protocols and earlier discharge, optimizing resource utilization. The use of dynamic biomarkers also underscores the importance of obtaining both preoperative and postoperative day 1 labs to inform risk stratification beyond static preoperative assessments. Although platelet count is used in SII, postoperative thrombocytosis or platelet activation could reflect reactive processes unrelated to inflammation.

Strengths and Limitations

Strengths of this study include a well-defined cohort with standardized timing of laboratory measurements, use of established reporting guidelines (TRIPOD, STROBE),[24,25] and rigorous internal validation via bootstrapping to correct for optimism. Although immunosuppressed patients were excluded, transient postoperative immunosuppression could still impact inflammatory biomarker readings.

However, several limitations warrant consideration. First, the retrospective single-center design may limit generalizability; practice patterns and patient demographics could differ elsewhere. We did not stratify complications by etiology (infectious vs non-infectious), which may have revealed different predictive patterns. Although the sample size allowed more than 10 events per variable, using seven predictors may still pose a risk of overfitting, particularly without external validation. Third, external validation in an independent cohort is needed before broad clinical implementation. Finally, we focused on early postoperative biomarker shifts (preoperative to day 1) and did not evaluate values on days 2 or 7 as predictors—future work could explore whether additional time points further enhance model performance. Despite internal validation, the model generalizability is not guaranteed; external cohort validation is essential. It is possible that elevated SII values reflect early subclinical infections rather than being purely predictive, warranting cautious interpretation.

Future Directions

Prospective, multicenter validation of our model is the logical next step to confirm generalizability and refine cutoff thresholds for clinical decision support. Incorporating dynamic markers into real-time risk calculators or mobile applications could facilitate bedside use. Further research might assess whether integration of other biomarkers (e.g., C-reactive protein, procalcitonin) or intraoperative variables (e.g., operative blood loss) augments predictive accuracy.[45-47] Finally, randomized trials could evaluate whether biomarker-guided perioperative care pathways translate into reduced complication rates, shorter hospital stays, and cost savings.

In this retrospective cohort of 260 patients undergoing cholecystectomy for acute calculous cholecystitis, we developed and internally validated a multivariable risk prediction model that integrates dynamic perioperative changes in liver function tests (ALT, AST, total bilirubin) and the SII with key clinical covariates. The final model demonstrated robust discrimination (optimism-corrected AUC, 0.82; 95% CI, 0.77–0.87) and excellent calibration (slope, 0.95; intercept, –0.02; Hosmer–Lemeshow p=0.45). Decision curve analysis confirmed clinical utility across threshold probabilities of 5% to 40%, with an estimated net gain of 15 true-positive identifications per 1 000 patients at a 20% threshold. However, external validation in independent populations is essential prior to clinical implementation. These findings suggest that routinely obtained perioperative biomarkers, when modeled dynamically, can meaningfully enhance early identification of patients at elevated risk for Clavien–Dindo grade≥II complications, thereby informing tailored perioperative management and optimizing resource allocation.

STATEMENT OF ETHICS

The study protocol was reviewed and approved by the Institutional Review Board of the Second Affiliated Hospital of Mudanjiang Medical University. Given the retrospective design and anonymized data extraction from electronic medical records, the requirement for individual informed consent was waived.

FUNDING

Not applicable.

CONFLICT OF INTEREST

The authors declare no conflicts of interest.

ACKNOWLEDGMENTS

Not applicable.

DATA AVAILABILITY

The de-identified dataset and analytic code supporting the conclusions of this article are available from the corresponding author upon reasonable request, subject to institutional and data-sharing agreements. R code and scripts used for analysis are available.

AI ASSISTANCE DISCLOSURE

None.

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