Association Between Preoperative Systemic Inflammation Response Index and Postoperative Recurrence in Patients With Intrahepatic Bile Duct Stones

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AIM: Intrahepatic bile duct stones (IHBDS) are characterized by a high postoperative recurrence rate. Their pathophysiological core lies in a vicious cycle of bile stasis, infection, and inflammation. Inflammatory responses play a crucial role in the onset, progression, and recurrence of IHBDS. This study aimed to evaluate the predictive performance of the preoperative systemic inflammation response index (SIRI) for postoperative recurrence in patients with IHBDS.

METHODS: This retrospective study analyzed 152 patients with IHBDS who underwent surgical resection between January 2018 and December 2024. Data, including demographic characteristics, comorbidities, and preoperative laboratory parameters, were collected. Receiver operating characteristic (ROC) curve analysis was used to determine the optimal cut-off values for the systemic immune-inflammation index (SII), SIRI, neutrophil-to-lymphocyte ratio (NLR), monocyte-to-lymphocyte ratio (MLR), and platelet-to-lymphocyte ratio (PLR). Furthermore, multivariate logistic regression analysis was performed to identify independent risk factors for postoperative recurrence.

RESULTS: ROC analysis demonstrated that SIRI had superior predictive performance compared with SII, NLR, MLR, and PLR, with an area under the curve (AUC) of 0.756 (95% confidence interval [CI]: 0.671–0.842). Multivariate analysis identified prior IHBDS-related surgical history (odds ratio [OR] = 3.06, 95% CI: 1.28–7.34, $p = 0.012$), preoperative SIRI (OR = 1.81, 95% CI: 1.21–2.72, $p = 0.004$), and total bilirubin level (OR = 1.07, 95% CI: 1.02–1.13, $p = 0.011$) as independent risk factors for postoperative recurrence.

CONCLUSIONS: Preoperative SIRI is a novel, independent, and readily detectable biomarker for predicting postoperative recurrence in patients with IHBDS. When combined with a history of prior biliary surgery and total bilirubin levels, SIRI can aid in risk stratification and guide surgical planning and postoperative management.

Keywords: intrahepatic bile duct stones; systemic inflammation response index; stone recurrence; prediction

Introduction

Intrahepatic bile duct stones (IHBDS) refer to primary calculi located proximal to the confluence of the right and left hepatic ducts, with a reported incidence of 2% to 25% in the Chinese population [1,2]. The typical clinical manifestations of IHBDS include abdominal pain, jaundice, and fever [3]. Its natural course is highly complex, often involving recurrent episodes of suppurative cholangitis, biliary strictures, and liver abscesses, and carries a substantial risk of progression to biliary cirrhosis and intrahepatic cholangiocarcinoma, posing a severe threat to long-term patient outcomes [4]. Despite advances in surgical techniques, including choledochotomy, hepatectomy, and laparoscopic bile duct exploration [5], studies demonstrate that the postoperative recurrence rate of IHBDS is affected by factors such as surgical methods and the presence of biliary stricture [6]. Thus, the postoperative recurrence rate of IHBDS remains unacceptably high and continues to represent a significant clinical challenge [1,7].

The chronic inflammatory state associated with IHBDS extends beyond localized biliary involvement and can trigger a systemic inflammatory response detectable in peripheral blood [8]. Inflammation-related biomarkers observed in complete blood count offer a simple and cost-effective means of evaluating systemic response. Among these, the neutrophil-to-lymphocyte ratio (NLR) has demonstrated prognostic value in predicting postoperative outcomes in patients with liver diseases [9,10]. However, the immunopathogenesis of IHBDS involves complex interactions among multiple immune cell types [11–13], and reliance on a single ratio may be inadequate to fully capture the intricacies of this immuno-inflammatory network.

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The systemic inflammation response index (SIRI), which integrates neutrophil, monocyte, and lymphocyte counts, is considered a comprehensive predictor of inflammation and immune status. It has been validated as a prognostic indicator for postoperative recurrence across various conditions [14–17]. By reflecting the balance between innate inflammatory responses driven by myeloid cells and adaptive immune responses mediated by lymphocytes [18–20], SIRI provides a widespread evaluation than single-cell-based ratios. However, its role in predicting postoperative recurrence of IHBDS has been rarely reported. This study systematically evaluated the association between SIRI and postoperative recurrence in patients with IHBDS, aiming to assess short-term clinical outcomes. Our results demonstrate that SIRI exhibits greater sensitivity and specificity than other indices in predicting the risk of recurrence.

Materials and Methods

Study Population

This retrospective cohort study included 152 patients with IHBDS who underwent surgery at Tangshan Gongren Hospital between January 2018 and December 2024, comprising 50 males and 102 females.

Inclusion and Exclusion Criteria

Inclusion criteria for patient selection were as follows: (1) age ≥18 years; (2) history of at least one surgical procedure for IHBDS; (3) confirmed diagnosis of intrahepatic bile duct stones based on preoperative imaging; and (4) availability of complete clinical and follow-up data.

Exclusion criteria included: (1) postoperative pathological confirmation of coexisting hepatocellular carcinoma; (2) presence of conditions affecting inflammatory markers, such as malignancies, autoimmune diseases, or hematologic disorders; (3) use of immunosuppressive agents or corticosteroids within two weeks before surgery; and (4) perioperative death.

Data Collection

Demographic and Baseline Characteristics: Data regarding age, sex, and body mass index (BMI) were recorded for all patients. Comorbidities related data included hypertension, diabetes mellitus, history of gallbladder stones, and prior IHBDS-related biliary surgery. Furthermore, overall health status was assessed using the Charlson Comorbidity Index (CCI) and the American Society of Anesthesiologists (ASA) physical status classification to evaluate surgical risk.

Disease- and Surgery-Related Clinical Features: Liver function was assessed using the Child–Pugh classification. Additional factors, such as intrahepatic stone distribution, surgical approach (with or without anatomical hepatectomy), intraoperative bile duct exploration, and T-tube placement, were also documented. Perioperative blood transfusion-related information was reported. Postoperative complications were graded using the Clavien–Dindo classification system, with grade ≥3 considered severe. Additionally, data regarding readmission within 30 days after surgery was recorded for each patient.

Laboratory Data: Clinical findings included hematological indices (platelet count, white blood cell (WBC) count, hemoglobin (Hb), red blood cell (RBC) count, neutrophil count, lymphocyte count, and monocyte count), liver function and biochemical indices (albumin, alanine aminotransferase (ALT), aspartate aminotransferase (AST), and total bilirubin (TBIL)), and coagulation parameters prothrombin time (PT) and international normalized ratio (INR).

Inflammatory Markers: Inflammatory markers documented were as follows: monocyte-to-lymphocyte ratio (MLR), platelet-to-lymphocyte ratio (PLR), neutrophil-to-lymphocyte ratio (NLR), systemic immune-inflammation index (SII) (platelet count × NLR), and SIRI (SIRI defined as neutrophil count × monocyte count/lymphocyte count).

Postoperative Stone Recurrence

For patients in whom complete stone clearance was confirmed by intraoperative choledochoscopy or postoperative imaging, recurrence was defined as the detection of newly formed stones on abdominal ultrasonography, computed tomography (CT), or magnetic resonance cholangiopancreatography (MRCP) at least 6 months after surgery. Cases with residual stones identified within <6 months postoperatively or early misdiagnoses were excluded. Recurrence time was calculated from the date of the initial surgery to the date of radiologic confirmation of recurrence.

Follow-up

All patients underwent CT and T-tube cholangiography before discharge to evaluate for residual stones. Post-discharge assessment included ultrasonography or CT scans every 3–6 months to monitor for intrahepatic or extrahepatic stone recurrence. Adherence to follow-up was high, with 95% of patients completing imaging at the scheduled intervals. However, 8 patients (5%) were lost to follow-up and were censored at the date of their last imaging.

Statistical Analysis

Statistical analyses were performed using SPSS software version 26.0 (IBM Corp., Armonk, NY, USA). The normality across continuous variables was assessed using the Shapiro–Wilk test. Variables following a normal distribution were expressed as mean ± standard deviation (Mean ± SD) and compared using the independent samples *t*-test. However, non-normally distributed data were presented as median with interquartile range (M, IQR), and group comparisons were assessed using the Mann–Whitney U test.

Categorical variables were reported as counts and percentages (n, %) and compared using the chi-square (χ^2) test or Fisher's exact test, as appropriate. Receiver operating characteristic (ROC) curves were plotted to evaluate the pre-

dictive performance of inflammatory indices (NLR, PLR, MLR, SII, and SIRI) for postoperative recurrence, with the area under the curve (AUC) and corresponding 95% confidence interval (CI) calculated. The optimal cut-off value for each index was determined using the Youden index. Due to significant data loss and the lack of regular parameter assessment in our clinical setting, specific potential confounding indicators (such as baseline infection status and biliary microbiota) were not included.

Furthermore, variables with statistical significance ($p < 0.05$) in univariate analysis were incorporated into a multivariate logistic regression model. Among inflammatory indicators (NLR, PLR, MLR, SII, SIRI), the AUCs were compared using the DeLong test, and the indicators with the highest predictive performance were selected for inclusion in the model. To reduce multicollinearity, variables highly correlated with the selected markers were excluded. Finally, the stepwise regression method was applied to identify independent predictors. Results were presented as odds ratios (ORs) with 95% CIs. All statistical tests were two-sided, and a p-value < 0.05 was considered statistically significant.

Results

Comparison of Baseline Characteristics and Clinical Outcomes Between the Non-recurrence and Recurrence Groups

A total of 152 patients who underwent surgery for IHBDS were included in the final analysis, among whom 48 (31.58%) developed postoperative recurrence. Demographic and clinical characteristics, including age, sex, BMI, Child–Pugh classification, or surgical approach, showed no statistically significant differences between the recurrence and non-recurrence groups (all $p > 0.05$). However, the history of prior IHBDS-related biliary surgery was significantly more common in the recurrence group compared to the non-recurrence group (43.75% vs. 20.19%, $p = 0.003$, Table 1).

Comparison of Laboratory Parameters and Systemic Inflammatory Markers in Patients With and Without Recurrent Liver Stones

Laboratory assessments further revealed substantial differences between the two groups. Patients with recurrence showed higher platelet counts, WBC, PT, and TBIL levels, along with lower albumin and hemoglobin levels (all $p < 0.05$, Table 2). Notably, all systemic inflammation-based biomarkers derived from peripheral blood counts—including the SII, SIRI, NLR, MLR, and PLR—were significantly elevated in patients with recurrence (all $p < 0.001$).

Predictive Performance of Inflammatory Markers for Postoperative Recurrence

To evaluate the predictive performance of preoperative systemic inflammatory status for postoperative recurrence, ROC curve analyses were performed for five inflammatory markers (Fig. 1). All markers demonstrated moderate predictive ability, with AUC ranging from 0.697 to 0.756.

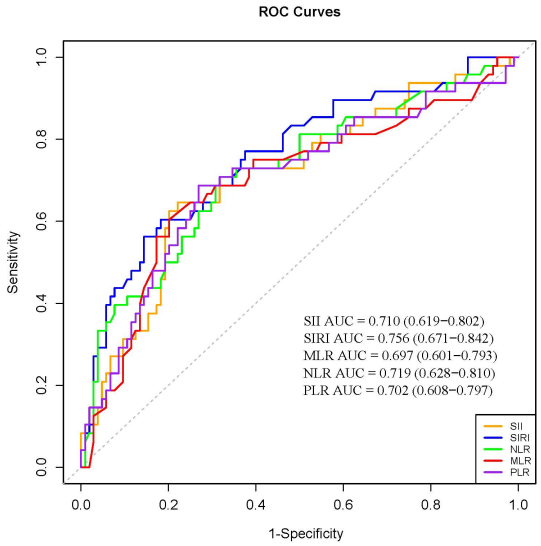

Fig. 1. ROC Curves of SIRI, SII, NLR, MLR, and PLR for Predicting Postoperative Recurrence in Hepatolithiasis Patients. ROC, Receiver operating characteristic; AUC, area under the curve; SII, systemic immune-inflammation index; SIRI, systemic inflammation response index; MLR, monocyte-to-lymphocyte ratio; NLR, neutrophil-to- lymphocyte ratio; PLR, platelet-to-lymphocyte ratio.

Comparison of AUCs using the DeLong test revealed SIRI as the optimal predictor. SIRI achieved the highest predictive performance, with an AUC of 0.756 (95% CI: 0.671–0.842). The optimal cut-off value for SIRI, determined by the maximum Youden index, was 3.140, corresponding to a sensitivity of 81.7% and a specificity of 60.4% for predicting postoperative recurrence (Table 3).

Independent Risk Factors for Postoperative Recurrence

Multivariate logistic regression analysis was conducted, incorporating clinically relevant variables and inflammatory markers selected by the DeLong test to reduce collinearity. Specifically, candidate variables with $p < 0.05$ in univariate analysis were initially included. Among multiple inflammatory markers (SII, SIRI, NLR, PLR, and MLR), SIRI showed the best discriminative performance based on ROC comparison and DeLong test and was therefore selected as the representative systemic inflammation marker. Notably, SIRI is calculated from neutrophil, lymphocyte, and monocyte counts, which are highly correlated; including these components individually could introduce multicollinearity. Three independent risk factors for postoperative recurrence were identified (Table 4): previous surgical history for IHBDS (OR = 3.06, $p = 0.012$), elevated preoperative SIRI (OR = 1.81, $p = 0.004$), and higher TBIL level (OR = 1.07, $p = 0.011$).

Table 1. Comparison of demographic characteristics between patients with recurrence and non-recurrence hepatic calculi.

Variable	Total (n = 152)	Non-recurrence (n = 104)	Recurrence (n = 48)	Statistic	*p*-value
Age (years), Mean ± SD	55.03 ± 19.45	55.61 ± 18.98	53.77 ± 20.57	$t = 0.54$	0.590
Sex, n (%)				$\chi^2 = 0.01$	0.938
Male	50 (32.89)	34 (32.69)	16 (33.33)		
Female	102 (67.11)	70 (67.31)	32 (66.67)		
BMI (kg/m^2), Mean ± SD	22.93 ± 5.09	22.73 ± 5.25	23.37 ± 4.74	$t = –0.72$	0.476
Hypertension, n (%)				$\chi^2 = 0.18$	0.674
No	127 (83.55)	86 (82.69)	41 (85.42)		
Yes	25 (16.45)	18 (17.31)	7 (14.58)		
Diabetes, n (%)				$\chi^2 = 1.21$	0.270
No	129 (84.87)	86 (82.69)	43 (89.58)		
Yes	23 (15.13)	18 (17.31)	5 (10.42)		
History gallstones, n (%)				$\chi^2 = 0.19$	0.664
No	104 (68.42)	70 (67.31)	34 (70.83)		
Yes	48 (31.58)	34 (32.69)	14 (29.17)		
Previous surgical history for IHBDS, n (%)				$\chi^2 = 9.11$	0.003
No	110 (72.37)	83 (79.81)	27 (56.25)		
Yes	42 (27.63)	21 (20.19)	21 (43.75)		
ASA score, n (%)				–	0.150
I	1 (0.66)	1 (0.96)	0 (0.00)		
II	138 (90.79)	97 (93.27)	41 (85.42)		
III	13 (8.55)	6 (5.77)	7 (14.58)		
CCI score, M (Q_1, Q_3)	3.00 (1.00, 6.00)	3.00 (1.00, 6.00)	3.00 (1.00, 6.25)	Z = –0.39	0.697
Child-Pugh, n (%)				$\chi^2 = 0.48$	0.489
A	141 (92.76)	98 (94.23)	43 (89.58)		
B	11 (7.24)	6 (5.77)	5 (10.42)		
Stone distribution, n (%)				$\chi^2 = 0.17$	0.683
Bilateral	51 (33.55)	36 (34.62)	15 (31.25)		
Unilateral	101 (66.45)	68 (65.38)	33 (68.75)		
Surgical method, n (%)				$\chi^2 = 0.56$	0.456
Laparoscopy	63 (41.45)	41 (39.42)	22 (45.83)		
Laparotomy	89 (58.55)	63 (60.58)	26 (54.17)		
Anatomical resection, n (%)				$\chi^2 = 0.54$	0.464
No	92 (60.53)	65 (62.50)	27 (56.25)		
Yes	60 (39.47)	39 (37.50)	21 (43.75)		
Biliary exploration, n (%)				$\chi^2 = 0.65$	0.420
No	61 (40.13)	44 (42.31)	17 (35.42)		
Yes	91 (59.87)	60 (57.69)	31 (64.58)		
T-tube drainage, n (%)				$\chi^2 = 0.21$	0.646
No	75 (49.34)	50 (48.08)	25 (52.08)		
Yes	77 (50.66)	54 (51.92)	23 (47.92)		
Perioperative blood transfusion, n (%)				$\chi^2 = 0.57$	0.449
No	135 (88.82)	91 (87.50)	44 (91.67)		
Yes	17 (11.18)	13 (12.50)	4 (8.33)		
Clavien–Dindo grade ≥ III, n (%)				$\chi^2 = 1.59$	0.207
No	123 (80.92)	87 (83.65)	36 (75.00)		
Yes	29 (19.08)	17 (16.35)	12 (25.00)		
Thirty day readmission, n (%)				$\chi^2 = 0.00$	0.979
No	130 (85.53)	89 (85.58)	41 (85.42)		
Yes	22 (14.47)	15 (14.42)	7 (14.58)		

Mean ± SD, mean ± standard deviation; M, median; Q_1, 1st Quartile; Q_3, 3rd Quartile. Abbreviations: BMI, body mass index; ASA, American Society of Anesthesiologists; CCI, Charlson Comorbidity Index; IHBDS, intrahepatic bile duct stones. – indicates the use of Fisher's exact test.

Table 2. Comparison of laboratory parameters and systemic inflammatory markers in patients with and without recurrent liver stones.

Variable	Total (n = 152)	Non-recurrent (n = 104)	Recurrent (n = 48)	Statistic	*p*-value
Laboratory test data					
Platelet (10^9/L), Mean ± SD	243.42 ± 105.64	225.01 ± 98.89	283.31 ± 109.75	t = –3.26	0.001
WBC (10^9/L), Mean ± SD	6.52 ± 1.38	6.28 ± 1.39	7.03 ± 1.23	t = –3.17	0.002
Hb (g/L), Mean ± SD	119.99 ± 19.32	122.57 ± 19.49	114.40 ± 17.91	t = 2.46	0.015
RBC (10^{12}/L), Mean ± SD	4.20 ± 0.61	4.27 ± 0.61	4.03 ± 0.56	t = 2.30	0.023
Neutrophil (10^9/L), M (Q_1, Q_3)	3.20 (2.40, 5.43)	2.90 (2.27, 5.00)	5.00 (2.98, 5.80)	Z = –3.97	<0.001
Lymphocyte (10^9/L), M (Q_1, Q_3)	1.60 (1.10, 2.30)	1.80 (1.20, 2.30)	1.15 (0.88, 1.72)	Z = –3.92	<0.001
Monocyte (10^9/L), M (Q_1, Q_3)	0.50 (0.40, 0.70)	0.40 (0.40, 0.60)	0.60 (0.47, 0.70)	Z = –3.08	0.002
Albumin (g/L), Mean ± SD	40.37 ± 4.75	41.09 ± 4.40	38.82 ± 5.14	t = 2.80	0.006
ALT (U/L), M (Q_1, Q_3)	63.10 (61.80, 64.00)	62.95 (61.70, 64.00)	63.35 (62.38, 64.20)	Z = –1.11	0.269
AST (U/L), M (Q_1, Q_3)	60.45 (59.38, 62.00)	60.60 (59.58, 61.82)	60.25 (59.00, 62.20)	Z = –0.55	0.580
TBIL (μmol/L), M (Q_1, Q_3)	20.10 (12.65, 24.52)	18.65 (11.55, 22.68)	24.05 (18.98, 32.23)	Z = –3.89	<0.001
PT (s), Mean ± SD	12.37 ± 1.18	12.18 ± 1.19	12.77 ± 1.06	t = –2.94	0.004
INR, Mean ± SD	1.29 ± 0.30	1.26 ± 0.29	1.35 ± 0.31	t = –1.71	0.089
Systemic inflammatory markers					
SII, M (Q_1, Q_3)	327.33 (179.81, 1618.77)	253.07 (162.89, 1309.88)	1545.68 (242.66, 2099.43)	Z = –4.16	<0.001
SIRI, M (Q_1, Q_3)	0.70 (0.41, 3.35)	0.57 (0.38, 2.71)	3.27 (0.76, 5.00)	Z = –4.77	<0.001
NLR, M (Q_1, Q_3)	1.82 (1.07, 5.02)	1.43 (1.00, 3.91)	4.67 (1.53, 6.23)	Z = –4.33	<0.001
MLR, M (Q_1, Q_3)	0.30 (0.17, 0.60)	0.22 (0.17, 0.48)	0.59 (0.28, 0.75)	Z = –3.90	<0.001
PLR, M (Q_1, Q_3)	116.51 (75.65, 299.42)	93.83 (66.16, 254.81)	279.31 (97.38, 381.85)	Z = –4.00	<0.001

Abbreviations: WBC, white blood cell; Hb, hemoglobin; RBC, red blood cell; ALT, alanine aminotransferase; AST, aspartate aminotransferase; TBIL, total bilirubin; PT, prothrombin time; INR, international normalized ratio; SII, systemic immune-inflammation index; SIRI, systemic inflammation response index; NLR, neutrophil-to-lymphocyte ratio; MLR, monocyte-to-lymphocyte ratio; PLR, platelet-to-lymphocyte ratio.

Table 3. ROC analysis of inflammatory markers for predicting postoperative recurrence.

Variable	AUC (95% CI)	Sensitivity	Specificity	Cut off	*p*-value
SII	0.710 (0.619–0.802)	77.9%	64.6%	1332.705	0.012
SIRI	0.756 (0.671–0.842)	81.7%	60.4%	3.140	-
NLR	0.719 (0.628–0.810)	68.3%	70.8%	2.896	0.007
MLR	0.697 (0.601–0.793)	79.8%	60.4%	0.516	<0.001
PLR	0.702 (0.608–0.797)	73.1%	68.8%	225.341	0.019

Abbreviations: AUC, area under the curve; CI, confidence interval; *p*-values denote the results of DeLong tests comparing each inflammatory marker with SIRI. SIRI is used as a reference indicator; therefore, SIRI does not show a *p*-value.

Discussion

This study is the first to systematically demonstrate that preoperative SIRI serves as an independent biomarker for predicting postoperative recurrence in IHBDS. This finding not only provides clinicians with a novel, simple, and practical tool for risk stratification but also offers new insights into understanding the pathophysiological mechanisms underlying IHBDS recurrence.

Through ROC curve analysis, we compared the predictive efficacy of SIRI with four other blood cell-derived inflammatory markers. SIRI achieved an AUC of 0.756 (95% CI: 0.671–0.842) and was confirmed as the best-performing biomarker by the Delong Test. However, its discriminatory ability when used as a single index remained only moderate.

The pathogenesis and progression of IHBDS represent a vicious cycle involving biliary obstruction, bacterial infection, and host immune response [4]. Previous research on IHBDS has primarily focused on markers such as NLR or SII [3], which overlooks the critical role of the monocyte-macrophage system in chronic liver inflammation and tissue remodeling. Monocytes serve as a crucial supplementary source of intrahepatic macrophages, which play key roles in mediating liver injury, amplifying inflammatory responses, and enhancing fibrosis [21].

Recent advances have highlighted the crucial role of neutrophil extracellular traps (NETs) in stone formation [22]. Upon stimulation by cholesterol crystals, bacterial lipopolysaccharide (LPS), and other triggers, neutrophils release NETs that trap and aggregate bilirubin, calcium and cholesterol microcrystals, thereby promoting stone formation [23,24]. Meanwhile, an elevated monocyte count contributes to hepatic infiltration, where they differenti-

Table 4. Multivariate logistic regression analysis of risk factors for postoperative recurrence in hepatolithiasis patients.

Variable	β	S. E	Wald	*p*-value	OR (95% CI)
Previous surgical history for IHBDS					
No					1.00 (Reference)
Yes	1.12	0.45	2.51	0.012	3.06 (1.28–7.34)
SIRI	0.60	0.21	2.88	0.004	1.81 (1.21–2.72)
Albumin	0.02	0.06	0.36	0.720	1.02 (0.90–1.16)
Platelet	0.00	0.00	0.27	0.784	1.00 (1.00–1.01)
TBIL	0.07	0.03	2.55	0.011	1.07 (1.02–1.13)
PT	0.13	0.25	0.53	0.596	1.14 (0.69–1.88)
RBC	–0.17	0.44	–0.39	0.695	0.84 (0.36–1.98)
Hb	0.01	0.02	0.38	0.706	1.01 (0.97–1.04)
Monocyte	–3.06	2.11	–1.45	0.147	0.05 (0.00–2.94)
WBC	–0.06	0.24	–0.26	0.795	0.94 (0.58–1.51)

OR, odds ratio; S. E, standard error.

ate into pro-inflammatory M1-type macrophages. These macrophages release a large amount of cytokines such as tumor necrosis factor-α (TNF-α), interleukin-1β (IL-1β), and interleukin-6 (IL-6), which aggravate hepatocyte and biliary epithelial cell injury, leading to periductal fibrosis and bile duct stricture formation [21]. Furthermore, IHBDS is often accompanied by biliary microbiota dysbiosis and bacterial infections, which produce β-glucuronidase, a key enzyme in the formation of pigment stone [25]. A decrease in lymphocytes indicates impaired immune clearance, limiting the host's ability to eliminate biliary infections or suppress the inflammatory response caused by innate immunity. Within this context, SIRI, an inflammatory indicator that simultaneously integrates neutrophil, monocyte and lymphocyte counts, offers a more comprehensive representation of the immune dysregulation underlying IHBDS.

The prognostic value of SIRI has been increasingly recognized across multiple diseases. Elevated SIRI levels have been closely associated with poor prognosis in gastrointestinal malignancies [26] and associated with an increased risk of gallstones (OR = 1.65, 95% CI: 1.12–2.43) [8]. Moreover, an National Health and Nutrition Examination Survey (NHANES)-based study involving 3295 subjects reported that when SIRI $<$ 1.42, it was positively correlated with the risk of gallstones [27]. Notably, the optimal cut-off value in that study was lower than the 3.140 observed in our study. This difference may stem from demographic differences, as the NHANES cohort primarily included participants under 50 years of age, whereas the average age of patients in our study was approximately 55 years. It is worth noting that in IHBDS, a benign but highly recurrent disease, there have been few previous reports on SIRI. To our knowledge, this study is the first to confirm its predictive value in IHBDS.

From a clinical perspective, the predictive value of SIRI extends beyond statistical associations and carries significant implications for patient management. Stratifying patients according to inflammatory status can identify patients with a high risk of recurrence, thereby providing a basis for individualized follow-up strategies, such as more frequent imaging monitoring and early detection of recurrence. For patients with SIRI $\geq$ 3.140, more aggressive intraoperative approaches or extended resection can also be considered to deal with occipital biliary stricture. Additionally, SIRI can assist in selecting patient groups who could benefit from adjuvant anti-inflammatory or microbial-targeted interventions. However, it should be emphasized that this cutoff value was derived from single-center data, and its universality requires validation in large, multi-center prospective studies. Despite this, incorporating SIRI into the preoperative risk assessment system offers practical and feasible means to refine risk stratification and optimize postoperative management pathways.

Besides SIRI, our multivariate logistic regression analysis identified two additional independent predictors of postoperative recurrence: a history of prior IHBDS-related biliary surgery and elevated preoperative TBIL levels. Among these, prior surgical history emerged as the strongest predictor. Patients requiring repeat surgeries are likely to have unresolved fundamental pathological factors from their initial operation, such as residual or complex intrahepatic biliary strictures or well-established biofilm-associated biliary dysbiosis [1]. These conditions perpetuate bile stasis and inflammatory stimuli, ultimately predisposing patients to recurrence. Elevated TBIL serves as a direct biochemical marker of cholestasis [28]. In cholestatic states, intrahepatic accumulation of toxic bile acids causes direct damage to hepatocytes and biliary epithelium [29]. This cellular injury triggers the release of abundant damage-associated molecular patterns [21], which act as endogenous danger signals to strongly activate Kupffer cells and infiltrating monocytes, inducing them to secrete pro-inflammatory mediators that further enhance neutrophil infiltration [21]. This, in turn, promotes postoperative recurrence in IHBDS patients.

Clinical Application of Predictive Models

In clinical practice, the identified independent variables—preoperative SIRI, TBIL, and prior IHBDS-related surgical history—can be incorporated into a simple risk assessment formula based on the multivariate logistic regression model:

$$\text{Logit}(P) = -3.21 + 1.11 \times \text{SIRI} + 0.07 \times \text{TBIL} + 1.12 \times \text{Prior Surgery}$$

Accordingly, a higher total score indicates a greater risk of postoperative recurrence. In practice, patients scoring above a defined threshold may be categorized as high-risk, requiring closer postoperative imaging surveillance and a more proactive surgical strategy. This approach enables clinicians to perform bedside risk stratification using routine laboratory and clinical data.

It is also worth noting that the study analyzed several clinically relevant factors, including surgical approaches, perioperative complications, and common comorbidities such as hypertension and diabetes; none of these factors showed a significant association with recurrence in our cohort. Although these findings should be interpreted with caution, given the limited sample size, they suggest that systemic inflammatory state may exert a more decisive impact on the risk of recurrence compared to the traditional variables.

In summary, preoperative SIRI demonstrates superior predictive performance for postoperative recurrence in IHBDS patients and holds potential as a biomarker for routine risk assessment. It may provide valuable guidance for individualized follow-up schedules and intervention strategies.

Limitations

Despite its promising outcomes, this study has several limitations. First, the retrospective design inherently introduces potential selection and information biases. Second, the single-center nature of the patient cohort may limit the generalizability of our findings, particularly in populations with different geographic or etiological backgrounds. In addition, the cutoff values reported in this study are derived from this single-center population and may be subject to overfitting; their applicability to other populations remains unclear and requires future validation in larger, multicenter cohorts. Third, residual confounding cannot be entirely excluded, as certain essential factors, such as comprehensive nutritional assessment, baseline infection conditions, and biliary microbiota profiles were not incorporated into the regression models. Moreover, stepwise regression was used to select variables, which, although widely employed, can lead to model instability and the potential omission of clinically important variables. Additional unmeasured confounders may also have affected the results; for example, the specific composition of the biliary microbiota was not evaluated, known lithogenic gene mutations were not analyzed, and medication use potentially influencing inflammatory markers was not comprehensively recorded. These limitations highlight the need for validation through future prospective, multi-center studies and consideration of more robust modeling strategies, such as penalized regression, to improve the reliability of the results.

Conclusions

This study demonstrates that preoperative SIRI serves as an effective biomarker for predicting postoperative recurrence in patients with IHBDS. Incorporating SIRI into preoperative risk assessment protocols may enhance surgical decision-making and guide personalized postoperative surveillance strategies.

Availability of Data and Materials

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

Author Contributions

MP, XY, LL and LZ contributed to the study design. MP conducted the literature search and performed data analysis. XY and LZ acquired the data. XY and MP wrote the article. LZ and LL 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 protocol was approved by the Medical Ethics Review Committee of Tangshan Gongren Hospital (Ethics Approval Number: 2024-016), with informed consent waived due to retrospective analysis of anonymized data. All procedures strictly adhered to the Declaration of Helsinki.

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Conflict of Interest

The authors declare no conflict of interest.

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