

Early Versus Late Laparoscopic Cholecystectomy After ERCP: A Comparative Study in Terms Intraoperative Adhesion Severity at a Single Center in Addis Ababa, Ethiopia from January 2023 to March 2026

Mikyas Befekadu Nigusse

mikyasbefekadun@gmail.com

MCM Comprehensive Specialized Hospital

Darrick L. Yeta

MCM Comprehensive Specialized Hospital

Michael Amare Atale

MCM Comprehensive Specialized Hospital

Sori Pawlos Gemechu

MCM Comprehensive Specialized Hospital

Tinsae Ketema Nurelign

MCM Comprehensive Specialized Hospital

Yeabsira Belete Kiros

MCM Comprehensive Specialized Hospital

Nehimia Kassa Hailemariam

MCM Comprehensive Specialized Hospital

Ashenafi B. Zelalem

Myungsung Medical College

Philimon Getu Bekele

MCM Comprehensive Specialized Hospital

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VI. Authors and Affiliations

Mikyas Befekadu Nigusse, MD (Intern) ^{1,3}

Darrick L. Yeta, MD (Intern) ^{1,3}

Michael Amare Atale, MD (Intern) ^{1,3}

Sori Pawlos Gemechu, MD (Intern) ^{1,3}

Tinsae Ketema Nurelign, MD (Intern) ^{1,3}

Yeabsira Belete Kiros, MD (General Practitioner) ^{2,3}

Nehimia Kassa Hailemariam, MD (Internist) ^{2,3}

Ashenafi B. Zelalem, MD, MPH (Health Data Scientist) ^{1,3}

Philimon Getu Bekele, MD (Surgeon) ^{1,3}

¹Department of General Surgery, MCM Comprehensive Specialized Hospital, Addis Ababa, Ethiopia

²Department of Internal Medicine, MCM Comprehensive Specialized Hospital, Addis Ababa, Ethiopia

³Myungsung Medical College, Addis Ababa, Ethiopia

All authors read and approved the final manuscript.

VII. Corresponding Author

Mikyas Befekadu Nigusse, MD (Intern) ^{1,2}

Email : mikyasbefekadun@gmail.com

VIII. Author contributions

Mikyas Befekadu Nigusse, MD (Intern): Conceived and designed the study, developed the study protocol, supervised the study, collected and analyzed the data, and drafted the manuscript.

26 **Darrick L. Yeta, MD (Intern):** Contributed to the study design and manuscript writing.

27 **Michael Amare Atale, MD (Intern):** Contributed to the study design, data analysis, and
28 interpretation of findings.

29 **Sori Pawlos Gemechu, MD (Intern):** Contributed to the study methodology, data analysis,
30 and manuscript drafting.

31 **Tinsae Ketema Nurelign, MD (Intern):** Contributed to data collection and interpretation of
32 the findings.

33 **Yeabsira Belete Kiros, MD (General Practitioner):** Contributed to the study methodology,
34 draft preparation, and critical revision of the manuscript.

35 **Nehimia Kassa Hailemariam, MD (Internist):** Contributed to the study methodology, draft
36 preparation, and critical revision of the manuscript.

37 **Ashenafi B. Zelalem, MD, MPH (Health Data Scientist):** Contributed to the study
38 methodology and critical revision of the manuscript.

39 **Philimon Getu Bekele, MD (Surgeon):** Contributed substantially to manuscript drafting,
40 academic writing, critical review, and revision of the manuscript.

41

IX. Abstract

Background: Laparoscopic cholecystectomy (LC) after endoscopic retrograde cholangiopancreatography (ERCP) is standard for gallstones with common bile duct stones, but the optimal ERCP-to-LC interval remains uncertain. This study assessed the association between the interval and intraoperative adhesion severity and operative difficulty

Objective: To compare early (≤ 72 hours) and late (> 72 hours) LC after ERCP with respect to intraoperative adhesion severity among patients treated at MCM Comprehensive Specialized Hospital, Addis Ababa.

Methods: A facility-based retrospective comparative cross-sectional study included 102 adults who underwent LC after ERCP for choledocholithiasis between January 2023 and March 2026. All eligible patients during the study period were included. Data were abstracted from medical records, ERCP reports, imaging, and operative notes and analyzed using SPSS v27. Adhesions were graded using the Zühlke classification, with grades II–IV considered severe. Binary and multivariable logistic regression were performed, reporting crude and adjusted odds ratios (AORs) with 95% CI. Robustness was assessed using a ≤ 6 -month interval and a log-transformed continuous ERCP–LC interval.

Results: Early LC was performed in 47 patients (46.1%) and late LC in 55 (53.9%), with a median ERCP–LC interval of 4 days. Severe adhesions were present in 59 patients (57.8%) and were more frequent following late LC than early LC (63.6% vs 51.1%; OR 1.68, 95% CI 0.76–3.71; $p=0.200$). On bivariate analysis, hydropic gallbladder was the only factor significantly associated with severe adhesions (OR 4.80; $p=0.024$). After adjustment for potential confounders, late LC was associated with higher odds of severe adhesions, although the association didn't reach statistical significance (AOR 2.39, 95% CI 0.95–6.01; $p=0.064$). In a sensitivity analysis excluding outlier, the association reached statistical significance (AOR 2.57; $p=0.047$). Furthermore, among patients undergoing LC within 6 months of ERCP, each log-unit increase in the ERCP–LC interval was associated with a 69% increase in the odds of severe adhesions (AOR 1.69, 95% CI 1.16–2.48; $p=0.007$).

Conclusion: A longer ERCP-to-LC interval was associated with denser intra-operative adhesions. The findings favor operating early after ERCP where circumstances allow, although the 72-hour mark is better read as a practical guide than as a fixed threshold.

72 **Key terms:** Laparoscopic cholecystectomy; ERCP; Minimally invasive surgery; Surgical
73 timing; Operative time; Intraoperative adhesions; Operative difficulty
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X. Background

Cholelithiasis is a common gastrointestinal disorder, with gallstones affecting approximately 6% of the global population (1). Among these, it is reported that 10-20% have concomitant CBD stones (2). Several approaches exist for this problem: preoperative ERCP followed by laparoscopic cholecystectomy (LC), intraoperative ERCP during LC, laparoscopic exploration of the duct, open surgery, or postoperative ERCP (3).

Laparoscopic cholecystectomy (LC) sits at the core of hepatobiliary surgery and has nearly replaced open surgery (4). Several factors contribute to the technical difficulty of laparoscopic cholecystectomy (LC), including patient-related, disease-related, and procedure-related factors. Among these, previous endoscopic retrograde cholangiopancreatography (ERCP) may independently increase the technical challenge of subsequent LC through local inflammation, edema, and tissue changes around the gallbladder and biliary tract (3, 5). Despite the widespread use of ERCP followed by LC for the management of choledocholithiasis, evidence regarding the optimal timing of LC after ERCP and its effect on surgical difficulty remains limited (6). Evidence at the global, African, and sub-Saharan African levels remains limited.

This study compared early (≤ 72 hours) and late (> 72 hours) laparoscopic cholecystectomy after ERCP in terms of severity of intra-operative adhesion among patients treated at MCM Comprehensive Specialized Hospital, Addis Ababa, Ethiopia, from 1 January 2023 to 30 March 2026.

XI. Methods

Study design, setting and aim

This study is a retrospective comparative cross-sectional study to assess the association between the timing of laparoscopic cholecystectomy (LC) after endoscopic retrograde cholangiopancreatography (ERCP) and intraoperative adhesion severity among adults with choledocholithiasis and cholelithiasis at MCM Comprehensive Specialized Hospital in Addis Ababa, Ethiopia. The study included 102 patients who underwent ERCP followed by LC between January 1, 2023, and March 30, 2026.

Participants

The study included all adult patients, aged 18 years and above, who had therapeutic ERCP with documented complete CBD stone clearance and subsequent laparoscopic cholecystectomy during the study period. Because all eligible records during the study period were reviewed, a census sampling approach was used. A total of 102 eligible patients were included in the final analysis, having 47 patients in the early LC group and 55 in the late LC group.

Study variables and outcome assessment

The primary outcome was the severity of intraoperative adhesions encountered during LC. Adhesions were graded according to the Zuehlke classification as grade 0, I, II, III, or IV. For the primary analysis, grades 0 and I were classified as non-severe adhesions, whereas grades II–IV were classified as severe adhesions (7). The dichotomy was based on the requirement for sharp dissection during adhesion lysis (8). The primary exposure was the timing of LC after ERCP, categorized as early (≤ 72 hours) or late (> 72 hours). We used the commonly applied 72-hour cutoff to define early and late LC, based on the subacute inflammatory changes that may occur after ERCP and contribute to adhesion formation (9, 10). The continuous ERCP-to-LC interval was also analysed in days and, in a sensitivity analysis, after logarithmic transformation. Potential predictors of severe adhesions included age, sex, previous upper-abdominal surgery, gallbladder condition, gallbladder wall thickness, CBD diameter, comorbidities, number of gallbladder stones and maximum gallstone size.

Data sources

Data were collected retrospectively from existing records using a structured, standardized, pretested abstraction checklist. Eligible cases were identified from ERCP logbooks in the GI unit, the operating-room registry, and the hospital medical record. For each patient, the ERCP report, anesthesia record, operative note, and imaging reports were reviewed.

Data Quality Control

- A structured and pretested data abstraction checklist was used.
- All study variables were clearly defined with standardized coding instructions.
- Operational definitions in the study protocol were followed consistently.

- Data collectors and supervisors received standardized training.
- A daily review of collected data for completeness and consistency was performed by supervisors and principal investigators.

Sample size

The sample size for comparing severe intraoperative adhesions between the two groups was determined using a two-population proportion formula, assuming severe adhesion rates of 45% among patients undergoing late LC and 25% among those undergoing early LC, based on a previous study (11). With 80% power, a 95% confidence level, and a two-sided test, the calculated sample size was 86 patients per group (172 in total). After allowing for 10% incomplete records, the final required sample size was 190 patients.

$$n = \frac{(Z_{\alpha/2} + Z_{\beta})^2 [p_1(1 - p_1) + p_2(1 - p_2)]}{(p_1 - p_2)^2}$$

$$n = \frac{(1.96 + 0.84)^2 [(0.45 \times 0.55) + (0.25 \times 0.75)]}{(0.45 - 0.25)^2} = \frac{7.84 \times 0.435}{0.04} = 85.3 \approx 86$$

This gives 86 patients per group, 172 in total, or 190 with the allowance ($172 \times 1.10 = 189.2$).

Legend of symbols

n: required sample size, per group for Objective 3 and in total for the others

$Z_{\alpha/2}$: standard normal deviate for a two-sided 95% confidence level ($\alpha = 0.05$), equal to 1.96

Z_{β} : standard normal deviate for 80% power, equal to 0.84

p: anticipated proportion, with p_1 and p_2 the proportions in the late and early LC groups

d: absolute precision, or margin of error, of the estimate

k: number of candidate predictor variables

EPV: Events per variable

However, given the retrospective design, a census sampling approach was adopted, whereby all patients meeting the inclusion criteria during the study period were considered for enrollment. Of these, complete data were available for 102 patients; due to missing or inaccessible records, this final cohort constituted the analytic sample.

Data Analysis

Data were analyzed using IBM SPSS Statistics version 27. Categorical variables were summarized using frequencies and percentages. Continuous variables were summarized using medians and interquartile ranges because the principal continuous variables were not normally distributed. The mean and standard deviations were additionally reported for age where appropriate.

Comparisons between early and late LC groups and between patients with severe and non-severe adhesions were performed using Pearson's chi-square test or Fisher's exact test for categorical variables, as appropriate. Continuous variables were compared using the Mann–Whitney U test. The ordinal Zuehlke adhesion grade was also compared using the Mann–Whitney U test, and the association between the ERCP-to-LC interval and adhesion grade was assessed using Spearman's rank correlation. Univariable binary logistic regression was used to calculate crude odds ratios (ORs) with 95% confidence intervals (CIs). Multivariable binary logistic regression was used to identify factors independently associated with severe adhesions. Variables with a bivariate p-value <0.25, together with the pre-specified exposure of LC timing, were considered for multivariable analysis. The final model was restricted according to the number of available severe-adhesion events to limit model instability. Adjusted odds ratios (AORs) with 95% CIs were reported.

Multicollinearity was assessed using the variance inflation factor. Model performance was evaluated using the likelihood-ratio test, Akaike information criterion, Bayesian information criterion, pseudo- R^2 statistics, area under the receiver-operating-characteristic curve, and Hosmer–Lemeshow goodness-of-fit test.

Missing data were not imputed. Variables with missing observations were analyzed using available cases, while the primary multivariable analysis used complete cases for the variables included in the model. A sensitivity analysis retained patients with missing measurements by including a separate “not recorded” category.

Additional sensitivity analyses examined the robustness of the association between LC timing and severe adhesions by excluding patients with ERCP-to-LC intervals >180 days and by modeling the interval as a log-transformed continuous variable.

All statistical tests were two-sided, and $p < 0.05$ was considered statistically significant. Associations with p -values between 0.05 and 0.10 were described as borderline and interpreted alongside their effect estimates and 95% CIs.

Post-hoc Power Analysis

Because the comparative objective was the one left short, power was calculated after the fact for its primary comparison, the difference in the proportion with severe adhesion between the early and late groups. The calculation used a two-sided test of two independent proportions at a 5% significance level, and the group sizes actually achieved were 47 early and 55 late.

On that basis, the study had about 25% power to detect the 12.6 percentage-point difference it in fact observed (63.6% versus 51.1%), and about 56% power to detect the 20-point difference assumed when the sample size was planned. The smallest difference detectable with 80% power was roughly 26 percentage points, confirming a difference of that size (Table 1).

A non-significant crude comparison is what these conditions predict; it is not evidence that no association exists. The comparison is accordingly interpreted through the direction and size of the effect, the width of its confidence interval, and the sensitivity and dose-response analyses. The multivariable model remains interpretable on its own terms, since it meets the events-per-variable requirement with 55 events across six predictors, although its confidence intervals are wide.

Table 1 Post-hoc power analysis for the primary comparison of severe adhesion (Zühlke grades II to IV) between early and late LC groups, computed for a two-sided test of two independent proportions at $\alpha = 0.05$

Parameter	Value	Interpretation
Significance level (α), two-sided	0.05	False-positive risk accepted
Design power target	80%	Conventional planning benchmark
Analysed sample (early / late)	102 (47 / 55)	Below the 190-patient target
Assumed difference ($p_1 - p_2$)	45% vs 25% (20 pts)	Basis of the a-priori sample size
Observed difference	63.6% vs 51.1% (12.6 pts)	Smaller than assumed
Power for the assumed 20-point difference	$\approx 56\%$	Even the planned effect was under-powered
Power for the observed 12.6-point difference	$\approx 25\%$	Chief reason the crude comparison reached only $p = 0.200$
Smallest difference detectable at 80% power	≈ 26 points	Only large effects were detectable
Sample required for the observed effect at 80% power	≈ 190 total (≈ 95 per group)	Target for a future definitive study

Power was computed for a two-sided test of two independent proportions at $\alpha = 0.05$ using the achieved group sizes. Percentage-point (pts) differences refer to the absolute difference in the proportion with severe adhesion (Zühlke grades II to IV) between the late and early groups.

Ethical Concerns

Ethical approval was obtained from the Institutional Review Board of MCM Comprehensive Specialized Hospital (Protocol No. PRO-060126). Beneficence was ensured by generating evidence to inform optimal surgical timing. Non-maleficence was upheld as the study involved retrospective review of patient records without direct patient contact. Autonomy was respected through an IRB-approved waiver of informed consent. Confidentiality was maintained by anonymizing all patient data and restricting data access to the research team only.

XII. Results

Patients' Characteristics

A total of 102 patients underwent therapeutic ERCP with documented clearance of common bile duct stones followed by laparoscopic cholecystectomy during the study period, and all of them were analyzed (Figure 1) due to the inadequate sample size.

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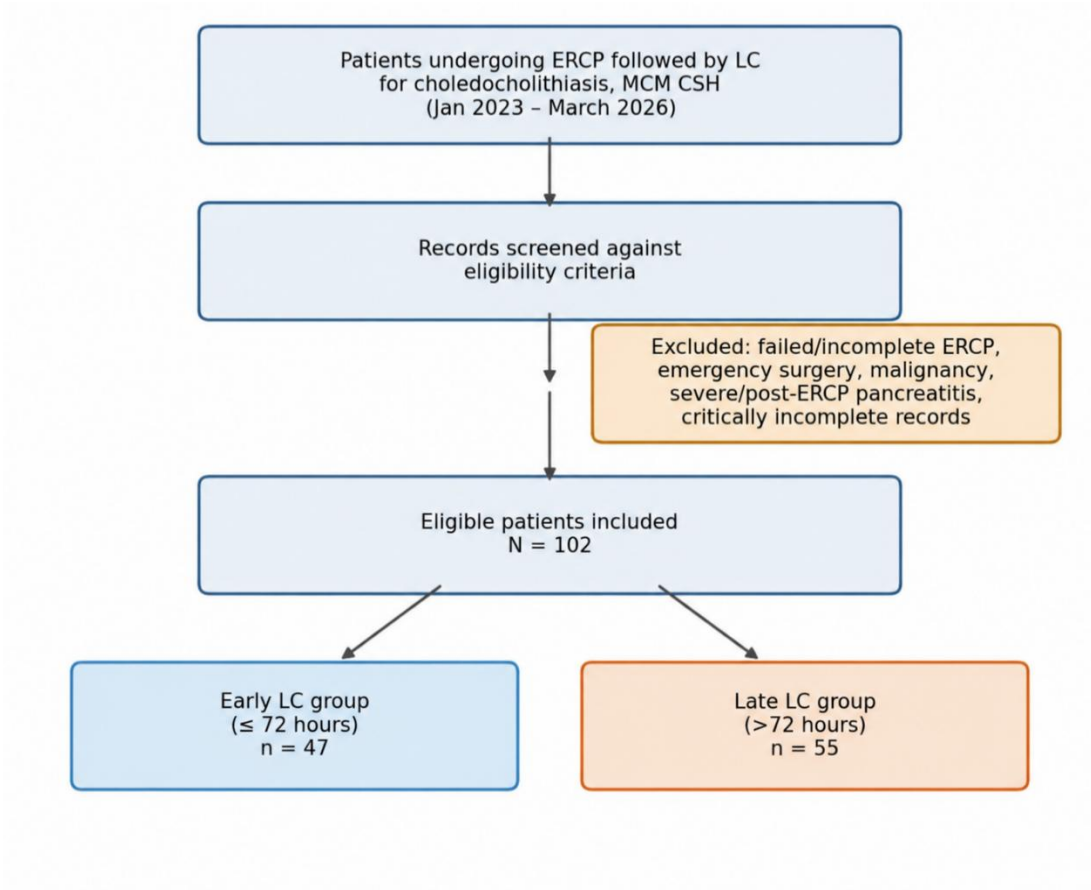


Figure 1 Flow diagram of patient selection and assignment to early and late cholecystectomy groups.

Women made up nearly two thirds of the patients 62.7% and men the remaining 37.3%, a female-to-male ratio of about 1.7 to 1. Median age 45 years (IQR 36 to 55), with a range of 24 to 75 years. Age was not evenly spread: patients clustered in two peaks, one from the late thirties to the mid-forties and a second in the early to mid-fifties. The sociodemographic characteristic across adhesion severity and timing of surgery (table 2). The clinical characteristics across adhesion severity and timing of surgery are shown (Table 3).

Table 2 Sociodemographic characteristics of the groups (N = 102), overall, by ERCP-LC timing and adhesion severity, MCM CSH, January 2023 to March 2026.

Characteristic	Total (N = 102)	By ERCP-LC timing		By adhesion severity	
		Early (n = 47)	Late (n = 55)	Non-severe (n = 43)	Severe (n = 59)
Age, years					
Median (IQR)	45 (36–55)	45 (36–54)	45 (36–58)	45 (31–54)	46 (39–58)
Range (min–max)	24–75	24–75	28–73	24–75	28–72
Sex, n (%)					
Female	64 (62.7)	29 (61.7)	35 (63.6)	31 (72.1)	33 (55.9)
Male	38 (37.3)	18 (38.3)	20 (36.4)	12 (27.9)	26 (44.1)

Table 3 Clinical characteristics of the groups (N = 102), overall, by ERCP-LC timing and adhesion severity, MCM CSH, January 2023 to March 2026.

Characteristic	Total (N = 102)	By ERCP-LC timing		By adhesion severity	
		Early (n = 47)	Late (n = 55)	Non-severe (n = 43)	Severe (n = 59)
Comorbidity, n (%)					
Diabetes mellitus	14 (13.7)	5 (10.6)	9 (16.4)	4 (9.3)	10 (16.9)
Hypertension	32 (31.4)	13 (27.7)	19 (34.5)	13 (30.2)	19 (32.2)
Prior upper-abdominal surgery	9 (8.8)	5 (10.6)	4 (7.3)	1 (2.3)	8 (13.6)
Stone burden, n (%)					
Single stone	20 (19.6)	8 (17.0)	12 (21.8)	11 (25.6)	9 (15.3)
Multiple stones	82 (80.4)	39 (83.0)	43 (78.2)	32 (74.4)	50 (84.7)
Gallbladder condition, n (%) ^b					
Normal	47 (47.0)	23 (48.9)	24 (45.3)	23 (54.8)	24 (41.4)
Sludge	20 (20.0)	7 (14.9)	13 (24.5)	10 (23.8)	10 (17.2)
Hydropic	18 (18.0)	9 (19.1)	9 (17.0)	3 (7.1)	15 (25.9)
Inflamed	15 (15.0)	8 (17.0)	7 (13.2)	6 (14.3)	9 (15.5)

Distribution of Adhesion and ERCP-to-LC Timing

The intraoperative adhesions across the study population were divided across all five Zuehlke grades, ranging from no grade 0 to grade IV) (Table 4). The study population was further divided according to the interval between ERCP and laparoscopic cholecystectomy, comprising early and late LC groups, with the distribution of patients between these two groups shown in (Figure 2).

Table 4 Distribution of adhesion grade (Zühlke classification) overall and by ERCP-LC timing.

Adhesion grade	Overall, n (%)	Early, n (%)	Late, n (%)
Grade 0 (no adhesions)	8 (7.8)	4 (8.5)	4 (7.3)
Grade I	35 (34.3)	19 (40.4)	16 (29.1)
Grade II	30 (29.4)	12 (25.5)	18 (32.7)
Grade III	19 (18.6)	9 (19.1)	10 (18.2)
Grade IV	10 (9.8)	3 (6.4)	7 (12.7)
Severe (Grade II-IV)	59 (57.8)	24 (51.1)	35 (63.6)

Ordinal grade by timing: Mann-Whitney $U = 1126$, $p = 0.245$. Severe vs non-severe by timing: $\chi^2 = 1.64$, $p = 0.200$

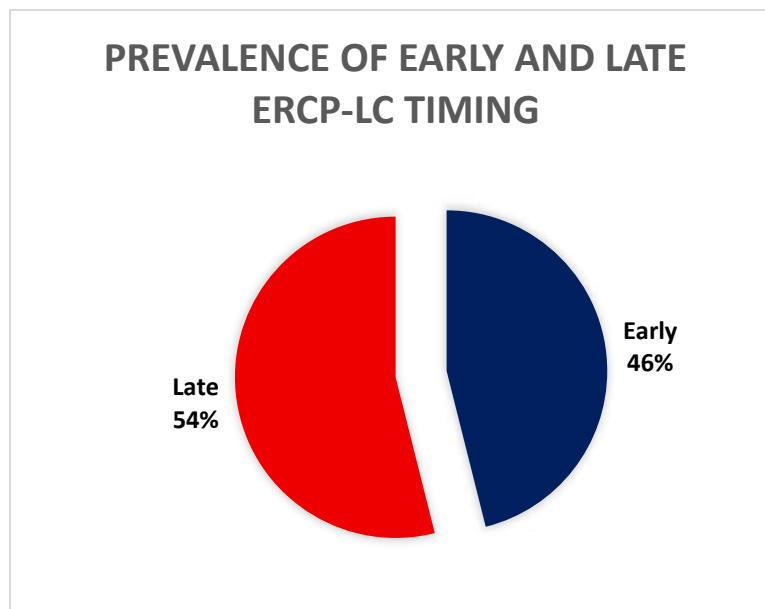


Figure 2 Distribution of ERCP-to-LC timing

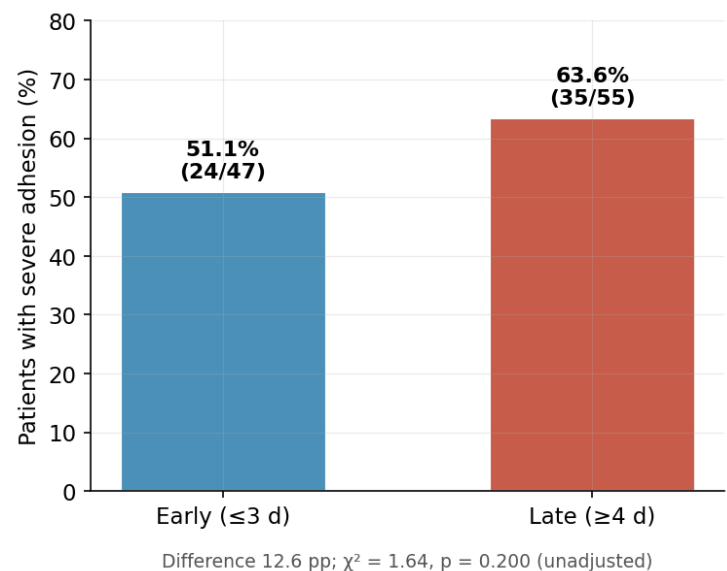


Figure 3 Proportion of severe adhesion by timing group

Association between Timing and severe adhesion

Severe adhesion was more common after late surgery (Figure 3). The difference did not reach statistical significance ($\chi^2 = 1.64$, $p = 0.200$; crude OR 1.68, 95% CI 0.76 to 3.71). The post-hoc power analysis indicated approximately 25% power to detect the observed effect. Comparing the ordinal Zuehlke grade rather than the dichotomy gave the same picture (Mann-Whitney $U = 1126$, $p = 0.245$), which indicates that splitting the outcome at grade II neither created nor concealed the association. The interval treated as a continuous variable pointed the same way: it correlated weakly with adhesion grade (Spearman $\rho = 0.171$, $p = 0.085$), and the median interval was longer in patients with severe adhesion than in those without (6 versus 3 days; Mann-Whitney $p = 0.109$).

Factors Associated with Severe Adhesion

On bivariate analysis, only hydropic gallbladder was significantly associated with severe intraoperative adhesions relative to a normal gallbladder (COR 4.80, 95% CI 1.23–18.71; $p = 0.024$). Several other variables trended in the anticipated direction without reaching significance (Table 5). After adjustment in the multivariable model, no factor retained statistical significance; however, delayed laparoscopic cholecystectomy showed a higher adjusted odds of severe adhesions that approached significance (AOR 2.40, 95% CI 0.96–6.01; $p = 0.061$) (Table 6).

Table 5 Bivariate analysis of factors associated with severe adhesion (crude odds ratios).

Variable	Category	Non-Severe (n=43)	Severe (n=59)	Crude OR (95% CI)	p-value
Age, mean (SD)	per year	44.4 (13.6)	48.4 (11.8)	1.03 (0.99-1.06)	0.118
Sex	Female	31	33	1.00 (ref)	0.098
	Male	12	26	2.04 (0.88-4.72)	
ERCP-LC Timing	Early (≤ 72 h)	23	24	1.00 (ref)	0.201
	Late (> 72 h)	20	35	1.68 (0.76-3.71)	
Prior Upper Abdominal Surgery	No	42	51	1.00 (ref)	0.081
	Yes	1	8	6.59 (0.79-54.81)	
Gallbladder wall thickness	≤ 3 mm	33	35	1.00 (ref)	0.076
	> 3 mm	8	20	2.36 (0.91-6.08)	
Gallbladder Condition	Normal	23	24	1.00 (ref)	
	Sludge	10	10	0.96 (0.34-2.72)	
	Hydropic	3	15	4.80 (1.23-18.71)	0.024
	Inflamed	6	9	1.44 (0.44-4.66)	
Multiple stones	Yes, vs single	32	50	1.91 (0.71-5.12)	0.199
Diabetes	Yes, vs no	4	10	1.99 (0.58-6.83)	0.274
Hypertension	Yes, vs no	13	19	1.10 (0.47-2.56)	0.832

Table 6 Multivariable logistic regression of factors associated with severe adhesion, showing the distribution of each predictor against the dependent variable with crude and adjusted odds ratio

Predictor	Category	Non-severe (n = 43)	Severe (n = 59)	COR (95% CI)	AOR (95% CI)	p-value
ERCP-LC timing	Early (≤ 72 h)	23 (53.5)	24 (40.7)	1.00 (reference)	1.00 (reference)	
	Late (> 72 h)	20 (46.5)	35 (59.3)	1.68 (0.76–3.71)	2.39 (0.95–6.01)	0.064
Prior upper-abdominal surgery	No	42 (97.7)	51 (86.4)	1.00 (reference)	1.00 (reference)	
	Yes	1 (2.3)	8 (13.6)	6.59 (0.79–54.81)	8.40 (0.89–79.63)	0.064
Sex	Female	31 (72.1)	33 (55.9)	1.00 (reference)	1.00 (reference)	
	Male	12 (27.9)	26 (44.1)	2.04 (0.88–4.72)	2.04 (0.80–5.20)	0.136
Gallbladder wall thickness ^a	≤ 3 mm	33 (80.5)	35 (63.6)	1.00 (reference)	1.00 (reference)	
	> 3 mm	8 (19.5)	20 (36.4)	2.36 (0.91–6.08)	2.14 (0.71–6.49)	0.179
Gallbladder condition ^b	Normal	23 (54.8)	24 (41.4)	1.00 (reference)	1.00 (reference)	
	Hydropic	3 (7.1)	15 (25.9)	4.80 (1.23–18.71)	2.55 (0.58–11.11)	0.214
Age (per year) ^c	Mean (SD)	44.4 (13.6)	48.4 (11.8)	1.03 (0.99–1.06)	1.02 (0.98–1.05)	0.369

Counts are n (column %) within each adhesion-severity group. The primary model was fitted on the 96 patients with complete data for all modelled variables (55 severe-adhesion events). Adjusted odds ratios are mutually adjusted for every predictor listed. ^a assessable in 96 patients; ^b recorded in 100 patients, with the sludge and inflamed categories entered only in the secondary model; ^c age is continuous, so the group columns give the mean (SD) rather than counts. Overall model: likelihood-ratio $\chi^2 = 17.06$, $df = 6$, $p = 0.009$; AUC = 0.716; Hosmer-Lemeshow $p = 0.590$; maximum VIF = 1.19.

Model Fit and Performance

The primary model fit the data significantly better than the null model, with modest explanatory power, acceptable discrimination, and good calibration; multicollinearity was negligible. A secondary model with additional covariates offered minimal improvement and did not alter the timing effect, and model selection criteria favored the more parsimonious primary model, which was retained for final analysis (Table 7).

Table 7 Fit and performance of the primary and secondary logistic models.

Statistic	Primary Refined Model	Secondary Full Model
Estimated coefficients (df)	6	10
Patients / severe events	96 / 55	96 / 55
Null deviance	131.04	131.04

Residual deviance	113.98	112.97
Likelihood-ratio χ^2 (p)	17.06 (0.009)	18.07 (0.054)
AIC / BIC	127.98 / 145.93	134.97 / 163.18
McFadden R²	0.130	0.138
Nagelkerke R²	0.219	0.230
Tjur R²	0.157	0.168
Discrimination (AUC)	0.716	0.731
Hosmer-Lemeshow χ^2 (p)	5.58 (0.590)	8.08 (0.425)
Maximum VIF	1.19	1.94

Primary model fit on 96 patients with complete wall-thickness data (55 severe events); secondary model on the same 96 patients

Sensitivity Analyses

Because the comparative objective fell short of its planned sample (47 early, 55 late), post-hoc power was calculated for the primary comparison. Power was ~25% to detect the observed 12.6-point difference (63.6% vs. 51.1%), and ~56% for the 20-point difference assumed at planning; 80% power would have required a difference of ~26 points. A non-significant crude result is therefore consistent with limited power rather than evidence against a true association, and the comparison is interpreted instead through effect direction and magnitude, confidence interval width, and sensitivity analysis.

Across sensitivity analyses adjusted for age, sex, prior upper-abdominal surgery, gallbladder wall thickness, and hydropic gallbladder, the association between delayed timing and severe adhesions remained consistent in direction and magnitude regardless of how missing wall-thickness data were handled. Whether extreme ERCP–LC intervals were excluded, or whether the interval was modeled continuously. The association reached statistical significance when extreme intervals were excluded and when analysis was restricted to intervals ≤ 180 days, suggesting outlier cases attenuated the crude estimate (Table 8).

Table 8 Sensitivity analyses for the timing effect on severe adhesion

Specification	n (events)	Effect Estimate (95% CI)	p-value
Primary model (complete-case)	96 (55)	2.39 (0.95-6.01)	0.064
All 102 via 'not recorded' wall category	102 (59)	2.23 (0.91-5.50)	0.081
Secondary full model	96 (55)	2.54 (0.98-6.59)	0.055
Excluding interval > 180 days	93 (54)	2.57 (1.01-6.54)	0.047

Continuous log-interval, full groups *	96 (55)	1.35 (0.99-1.83)	0.056
Continuous log-interval, ≤ 180 days*	93 (54)	1.69 (1.16-2.48)	0.007

Odds ratios per one-unit increase in the log-transformed interval (continuous exposure). Timing odds ratios are for late (>72h) versus early (≤72h) surgery.

XIII. Discussion

ERCP has long been the primary definitive treatment for common bile duct stones. Since its onset, it has become a standard approach for biliary stone clearance (12, 13). Following successful ERCP, laparoscopic cholecystectomy (LC) is recommended to prevent recurrent biliary events. However, the optimal timing of LC, whether early or delayed, remains controversial, and no universally accepted consensus has been established (12). ERCP itself may induce inflammation and edema around Calot's triangle, potentially increasing the technical difficulty of subsequent LC. Therefore, some authors recommend that the procedure be performed by experienced surgeons, particularly when significant inflammation is anticipated (3, 5).

How difficult any LC turns out to be depends on several things: inflammation (acute or chronic), a gallbladder wall thicker than 3 mm, distension, history of upper abdominal surgery, anatomy variations, and most reliably adhesions (14). Adhesions obscure key landmarks, demand more dissection, lengthen the operation, increase blood loss and the risk of iatrogenic injury, hinder achievement of the critical view of safety, and make conversion to open surgery more likely (7, 15).

Baseline Characteristics and Intraoperative Adhesion Severity

The baseline demographic and clinical characteristics were comparable between the early and late LC groups, with no statistically significant differences in age, sex, comorbidities including diabetes and hypertension, gallbladder condition, and biliary tract characteristics. These findings are consistent with those reports that found no significant differences between early and late LC groups (9, 15, 16). Overall, the similarity in baseline characteristics observed in the present study supports the comparability of the two groups, reducing the likelihood that differences were attributable to baseline characteristics. The study was limited by its relatively small sample size and consequently low statistical power. The post-hoc analysis suggested approximately 25%

power to detect the observed difference in severe adhesions between groups, increasing the possibility of a type II error. Therefore, the absence of statistical significance should be interpreted cautiously and does not necessarily indicate the absence of an association.

Male sex showed roughly two-fold higher odds of severe adhesion, though not significant, consistent with reports of more technically difficult cholecystectomy and higher conversion in men, possibly reflecting later presentation or more advanced disease (17). Older age showed a weak, non-significant association that disappeared after adjustment, in line with evidence that age affects operative difficulty mainly through frailty and comorbidity rather than directly. Neither factor was independently associated with severe adhesion in this study (18).

Adhesion severity was assessed intraoperatively using the Zuehlke classification, which grades adhesions from Grade 0 to Grade IV. Grades II–IV were considered severe adhesions, indicating increasing difficulty requiring sharp dissection (19). More than half of the patients (57.8%) had severe adhesions (Zuehlke grade II–IV), and only a small proportion had no adhesions (7.8%), indicating a substantial adhesion burden in post-ERCP cases. These findings highlight that these patients frequently present with technically challenging operations in which adhesions may obscure Calot’s triangle, complicate dissection, prolong surgery, and increase operative difficulty as well as the risk of intraoperative injury (3, 5). Consistent with the literature, laparoscopic cholecystectomy after ERCP is widely recognized as being associated with increased adhesion formation due to inflammation-related fibrosis, bacterial colonization, and duodenobiliary reflux, which might make the procedure difficult (3, 7).

When stratified by timing of surgery in the present study, severe adhesions were more frequent in the late surgery group compared with the early group (63.6% vs 51.1%). This can be explained by a time-dependent progression of inflammatory changes and fibrotic adhesion formation following ERCP (3).

Although severe adhesions were already common in the early group, the higher proportion observed in late surgery indicates increasing operative complexity with longer ERCP–LC intervals. This finding aligns with previous studies, including a prospective comparative study from India, which similarly reported significantly higher severe adhesions in late laparoscopic cholecystectomy compared with early surgery, reinforcing the concept that postponing surgery after ERCP is associated with progressive inflammation and fibrosis, ultimately increasing operative difficulty (20).

Factors Associated with Adhesion Severity

Several clinically relevant factors were studied with severe intra-operative adhesion, including both patient-related and disease-related factors. Among these, prior abdominal surgery showed no significant association. The condition of the gallbladder at the time of LC may influence operative difficulty. Acute inflammation, gallbladder distension (hydrops), and increased wall thickness can lead to tissue edema, friability, and dense adhesions, making dissection more challenging (15).

A hydropic gallbladder was significantly associated with severe adhesions on bivariate analysis, suggesting a strong relationship between gallbladder distension and adhesion formation. However, this association lost statistical significance after adjustment for other variables, despite patients with a hydropic gallbladder remaining nearly twice as likely to develop severe adhesions. This attenuation may indicate that the observed association was partly explained by related inflammatory features, such as gallbladder wall thickening and other clinical characteristics. Nevertheless, the finding remains clinically relevant and consistent with the known association between gallbladder distension and underlying inflammatory tissue changes, which may increase technical difficulty during laparoscopic cholecystectomy (3).

Late LC was associated with approximately 2.4-fold higher odds of severe adhesions, although the association did not reach statistical significance. However, the association became significant in the sensitivity analyses. This suggests that the primary analysis may have been limited by the study's low statistical power and the highly skewed distribution of the ERCP–LC interval. The consistent direction of the association across analyses supports a true relationship between late surgery and adhesion severity. After a 6-month cutoff was used, which is considered a benchmark for recurrence, the values were significant (21). In this study, as time passed, severity of adhesion progressively increased. Delaying LC allows progressive inflammation, fibrin organization, and fibrosis to occur. These changes promote denser pericholecystic adhesions and increase operative difficulty. This interpretation is consistent with previous studies reporting that late LC after ERCP is associated with more severe adhesions and more technically demanding surgery (16, 20).

Although prior abdominal surgery was associated with approximately eightfold higher odds of severe adhesions, this association did not reach statistical significance. This finding contrasts with the well-established mechanism whereby postoperative peritoneal injury disrupts normal tissue planes and promotes adhesion formation. However, the lack of statistical significance should be

394 interpreted cautiously, given the limited sample size and low statistical power of the study. The
395 post-hoc power analysis indicated approximately 25% power to detect the observed association,
396 suggesting a substantial possibility of a type II error (14).

397 This is, to our knowledge, one of the first Ethiopian studies and among the few from sub-
398 Saharan Africa to evaluate ERCP-to-LC timing in relation to adhesion severity and operative
399 difficulty. The paucity of comparable regional data limits direct comparison; however, this also
400 underscores the importance of the present findings, as they contribute locally generated evidence
401 from a setting where outcomes following post-ERCP laparoscopic cholecystectomy are rarely
402 documented. Such evidence may inform operative planning, patient counselling, and decision-
403 making regarding the timing of laparoscopic cholecystectomy after ERCP, particularly in
404 resource-limited settings where surgical expertise and equipment constraints may influence
405 outcomes.

406

XIV. Conclusion

In this single-center Ethiopian study, a longer ERCP-to-LC interval was associated with more severe intra-operative adhesions. Severe adhesion affected 57.8% of patients. A hydropic gallbladder was the only factor significantly associated with severe adhesion individually. Late timing, prior upper-abdominal surgery, a thickened gallbladder wall, and male sex all pointed in the same direction after adjustment, without reaching significance individually. The model's limited power to detect these individual associations likely reflects the modest sample size rather than an absence of true effect. The consistency of direction across predictors lends some support to the overall pattern despite the lack of individual significance. The ability to detect these individual associations was limited by the modest sample size. The post-hoc analysis estimated approximately 25% power to detect the observed effect, indicating a substantial risk of type II error. Thus, the lack of statistical significance for some predictors should not necessarily be interpreted as evidence of no association, particularly given the consistency of effect direction across predictors. The timing association was borderline in the full sample and significant once the three patients who operated beyond six months were set aside, and the continuous analysis showed a dose-response consistent with it. On this evidence, operating earlier after ERCP is likely to make the operation easier where circumstances allow, though the 72-hour mark is better treated as a practical guide than as a threshold with any special biological meaning.

XV. Limitation and Generalizability

This was a retrospective, single-center study, which limits generalizability and leaves room for confounding and selection bias — particularly since findings from a single tertiary hospital may not translate to public or lower-resource settings with different patients and referral patterns. Several estimates are imprecise due to wide confidence intervals from small event counts. Most notably, the study was underpowered: the achieved sample of 102 fell short of the 190 needed for the primary between-group comparison, so results should be interpreted through effect size and consistency of direction rather than statistical significance alone.

Abbreviations

AIC, Akaike Information Criterion; AOR, Adjusted Odds Ratio; AUC, Area Under the Curve; BIC, Bayesian Information Criterion; CBD, Common Bile Duct; CI, Confidence Interval; CVS, Critical View of Safety; EPV, Events Per Variable; ERCP, Endoscopic Retrograde Cholangiopancreatography; EUS, Endoscopic Ultrasonography; IQR, Interquartile Range; IRB, Institutional Review Board; LC, Laparoscopic Cholecystectomy; MCM CSH, MCM Comprehensive Specialized Hospital; MRCP, Magnetic Resonance Cholangiopancreatography; OR, Odds Ratio; SD, Standard Deviation; SPSS, Statistical Package for the Social Sciences; VIF, Variance Inflation Factor.

XVI. Declaration

Competing interests

The authors declare that they have no competing interests.

Consent for publication

Not applicable. This study did not include any individual-level identifiable information, images, or other material requiring consent for publication.

Availability of data and materials

The datasets generated and/or analyzed during the current study are not publicly available due to institutional and patient confidentiality requirements but may be available from the corresponding author upon reasonable request and subject to appropriate institutional approval.

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Authors contribution

MBN conceived and designed the study, developed the study protocol, supervised the study, collected and analyzed the data, and drafted the manuscript. DLY contributed to the study design and manuscript writing. MAA contributed to the study design, data analysis, and interpretation of findings. SPG contributed to the methodology, data analysis, and manuscript drafting. TKN contributed to data collection and interpretation of the findings. YBK and NKH contributed to the study methodology, draft preparation, and critical revision of the manuscript. ABZ contributed to the study methodology and critical revision of the manuscript. PGB contributed substantially to manuscript drafting, academic writing, critical review, and revision of the manuscript. All authors reviewed and approved the final manuscript and agreed to be accountable for all aspects of the work.

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STROBE guidelines

This study was reported in accordance with the Strengthening the Reporting of Observational Studies in Epidemiology (STROBE) guidelines. The completed STROBE checklist is provided as a supplementary file.

Reference

1. Wang X, Yu W, Jiang G, Li H, Li S, Xie L, et al. Global Epidemiology of Gallstones in the 21st Century: A Systematic Review and Meta-Analysis. Clin Gastroenterol Hepatol. 2024;22(8):1586-95.

2. Saito H, Kadono Y, Shono T, Kamikawa K, Urata A, Nasu J, et al. Remaining issues of recommended management in current guidelines for asymptomatic common bile duct stones. *World J Gastroenterol.* 2021;27(18):2131-40.
3. Reinders JSK, Gouma DJ, Heisterkamp J, Tromp E, van Ramshorst B, Boerma D. Laparoscopic cholecystectomy is more difficult after a previous endoscopic retrograde cholangiography. *HPB.* 2013;15(3):230-4.
4. Asad U, Wang CF, Jones MW. Laparoscopic Cholecystectomy. StatPearls. Treasure Island (FL): StatPearls Publishing Copyright © 2025, StatPearls Publishing LLC.; 2025.
5. Kaushik R. Bleeding complications in laparoscopic cholecystectomy: Incidence, mechanisms, prevention and management. *J Minim Access Surg.* 2010;6(3):59-65.
6. El Nakeeb A, Sultan AM, Hamdy E, El Hanafy E, Atef E, Salah T, et al. Intraoperative endoscopic retrograde cholangio-pancreatography: a useful tool in the hands of the hepatobiliary surgeon. *World J Gastroenterol.* 2015;21(2):609-15.
7. Kapoor A, Sidhu BS, Singh J, Brar N, Singh P, Kapur A. Adhesions Detection and Staging Classification for Preoperative Assessment of Difficult Laparoscopic Cholecystectomies: A Prospective Case-Control Study. *J Med Ultrasound.* 2023;31(2):137-43.
8. Ten Broek RPG, Krielen P, Di Saverio S, Coccolini F, Biffl WL, Ansaloni L, et al. Bologna guidelines for diagnosis and management of adhesive small bowel obstruction (ASBO): 2017 update of the evidence-based guidelines from the world society of emergency surgery ASBO working group. *World J Emerg Surg.* 2018;13:24.
9. Lau JY, Leow CK, Fung TM, Suen BY, Yu LM, Lai PB, et al. Cholecystectomy or gallbladder in situ after endoscopic sphincterotomy and bile duct stone removal in Chinese patients. *Gastroenterology.* 2006;130(1):96-103.
10. Poprom N, Suragul W, Muangkaew P, Vassanasiri W, Rungsakulkij N, Mingphruedhi S, et al. Timing of laparoscopic cholecystectomy after endoscopic retrograde cholangiopancreatography in cholelithiasis patients: A systematic review and meta-analysis. *Ann Hepatobiliary Pancreat Surg.* 2023;27(1):20-7.
11. Ali RF, Aouf A, Isamil K, Ismail T, Elbatae H. Randomized Controlled Clinical Trial of Early vs Delayed Laparoscopic Cholecystectomy after CBD Stone Clearance. *Indian Journal of Surgery.* 2021;83(5):1158-65.
12. Kozarek RA. The Past, Present, and Future of Endoscopic Retrograde Cholangiopancreatography. *Gastroenterol Hepatol (N Y).* 2017;13(10):620-2.
13. Abdo A, Dafalla S, Bushra M, Mustafa R, Hamad R, Rafei A, et al. Endoscopic retrograde cholangiopancreatography services in Sudan during wartime: Innovations in crisis. *Endosc Int Open.* 2025;13:a26215666.
14. Sugrue M, Sahebally SM, Ansaloni L, Zielinski MD. Grading operative findings at laparoscopic cholecystectomy- a new scoring system. *World Journal of Emergency Surgery.* 2015;10(1):14.
15. Manatakis DK, Antonopoulou MI, Tasis N, Agalianos C, Tsouknidas I, Korkolis DP, et al. Critical View of Safety in Laparoscopic Cholecystectomy: A Systematic Review of Current Evidence and Future Perspectives. *World J Surg.* 2023;47(3):640-8.
16. Salman B, Yılmaz U, Kerem M, Bedirli A, Sare M, Sakrak O, et al. The timing of laparoscopic cholecystectomy after endoscopic retrograde cholangiopancreaticography in cholelithiasis coexisting with choledocholithiasis. *Journal of Hepato-Biliary-Pancreatic Surgery.* 2009;16(6):832-6.

17. Zisman A, Gold-Deutch R, Zisman E, Negri M, Halpern Z, Lin G, et al. Is male gender a risk factor for conversion of laparoscopic into open cholecystectomy? *Surg Endosc*. 1996;10(9):892-4.
18. Chandio A, Timmons S, Majeed A, Twomey A, Aftab F. Factors influencing the successful completion of laparoscopic cholecystectomy. *Jsls*. 2009;13(4):581-6.
19. Sönmez S, Akselim B, Karaşin SS. The effectiveness of preoperative diagnostic methods in predicting intra-abdominal adhesions before repeat cesarean section delivery. *Rev Assoc Med Bras (1992)*. 2023;69(4):e20221455.
20. Dr Devang J, Dr Lakshman A, Dr Umar F, Dr Rounak C. Comparative Analysis of Early Versus Late Laparoscopic Cholecystectomy Following Endoscopic Retrograde Cholangiopancreatography in Cases of Cholelithiasis with Choledocholithiasis. *International Journal of Pharmacy Research & Technology (IJPRT)*. 2026;16(1):1-4.
21. Mansour S, Kluger Y, Khuri S. Primary Recurrent Common Bile Duct Stones: Timing of Surgical Intervention. *J Clin Med Res*. 2022;14(11):441-7.