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Original Article

Application of Intraoperative Indocyanine Green Fluorescence to Decrease Length of Stay in the Difficult LC Patients in Buddhachinaraj Hospital, Phitsanulok

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ABSTRACT

Background: Laparoscopic cholecystectomy (LC) is currently widely used for the treatment of gallstone disease. In Thailand, studies on the use of ICG to assist LC in patients with difficult LC remain limited. The researchers therefore believe that this study will help clarify the benefits of using indocyanine green (ICG)-assisted laparoscopic cholecystectomy (ICG-FC LC) in patients with difficult LC, and will also serve as a data source for future research development.

Objective: To compare the postoperative length of hospital stay (as a primary indicator of surgical efficiency and postoperative recovery) between ICG-FC LC and conventional LC in patients with difficult LC due to biliary stone disease, between January 1, 2020, and December 31, 2025.

Materials and Methods: A cohort observational ambispective study involving patients aged ≥18 years diagnosed with difficult or very difficult LC based on the scoring system of the modified Randhawa's model by Tongyoo et al., and underwent treatment at Buddhachinaraj Hospital between 2020 and 2025. Surgery was performed by a single surgeon. A total of 168 patients met the eligibility criteria. The first group consisted of patients scheduled for elective LC (defined as delayed or interval procedures performed after the clinical resolution of acute inflammatory symptoms) (ICG group; n = 84) between January 1, 2025, and December 31, 2025. The second group consisted of patients selected via convenience sampling (non-ICG group; n = 84) between January 1, 2020, and December 31, 2024. Clinical outcomes—including length of hospital stay, drain placement rate, conversion rate, intraoperative blood loss, operative time, and surgery-related complications—were compared. Statistical analyses were performed using Student's t-test, Chi-square test, Fisher's exact test, quantile regression for continuous outcomes, and modified Poisson regression for categorical outcomes to adjust for confounders.

Results: The ICG-FC LC group demonstrated a significantly shorter postoperative length of stay compared with the conventional LC group (median 1.4 vs. 2.1 days; adjusted median difference −0.62 days, 95% CI

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−1.23 to −0.01; p = 0.047). Intraoperative blood loss (18.3 vs. 27.0 mL; p < 0.001) and operative time (99.0 vs. 114.0 minutes; p < 0.001) were also significantly lower in the ICG group. Drain placement rate, conversion rates, and complication rates were comparable between groups. Among patients with difficult LC, ICG-FC LC resulted in a significantly shorter length of stay (1.3 vs. 1.9 days; adjusted median difference −0.6 days, 95% CI −0.9 to −0.3; p < 0.001) and reduced intraoperative blood loss (9.9 vs. 25.1 mL; p < 0.001). In very difficult LC cases, no statistically significant differences were observed in length of stay, although a trend toward shorter length of stay was noted in the ICG group (2.0 vs 3.4 days, p = 0.125). Conversely, intraoperative blood loss was significantly higher in the ICG group among very difficult cases (70.3 vs. 31.6 mL; p = 0.008).

Conclusion: ICG-FC LC was associated with a shorter postoperative length of stay and reduced intraoperative blood loss while maintaining comparable conversion rates and postoperative complications relative to conventional LC. These findings suggest that ICG fluorescence cholangiography appears to be generally safe in selected difficult LC cases, although its benefits may be physically limited in very difficult procedures.

Keywords: Laparoscopic cholecystectomy, Difficult laparoscopic cholecystectomy, Indocyanine green fluorescence cholangiography, Surgical outcomes

Introduction

Gallstone disease is one of the most common causes of abdominal pain and may lead to various complications. Currently, laparoscopic cholecystectomy (LC) is widely performed as the standard treatment for gallstone disease. Although advances in laparoscopic surgical skills and instrumentation have significantly improved outcomes, difficult LC cases remain challenging for surgeons due to prolonged operative time and higher complication rates. Based on patient data collected at Buddhachinaraj Hospital, Phitsanulok, between 2016 and 2022, approximately 200 to 300 LC procedures were performed annually. As cholecystectomy at Buddhachinaraj Hospital is generally performed as elective LC (typically scheduled after the acute phase of inflammation has resolved) rather than early LC, the likelihood of encountering difficult LC cases characterized by dense retrocholecystic fibrosis and altered anatomy is therefore increased.

The Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) recommends the use of the Critical View of Safety (CVS) during LC to reduce the risk of bile duct injury.[1] Despite the implementation of CVS within safe LC surgery protocols, operative complications remain a major concern as they can be life-threatening or lead to prolonged hospital stay, increased healthcare-associated costs, and a need for reinterventions or additional procedures.[2-5] These injuries often arise from unclear anatomy or anatomical variations.[6-8] In some patients, inflammation of the gallbladder or biliary tract may result in fibrosis around Calot's triangle, making it difficult to achieve CVS.[6,7,9]



To preoperatively stratify the surgical risk, various scoring systems have been developed. While the Tokyo Guidelines (TG18)[10] are globally accepted for assessing the severity of acute cholecystitis, this study utilized the modified Randhawa's scoring system.[11-15] This model was specifically selected because it incorporates a broader range of preoperative clinical and radiological parameters to predict the technical difficulty of elective LC across various complex pathologies, including post-inflammatory scarring and contracted gallbladders, rather than solely focusing on acute inflammation.

Intraoperative cholangiography is a technique that enhances visualization of the extrahepatic biliary system during LC.[16] The indocyanine green (ICG) is a relatively safe fluorescent dye predominantly metabolized by the liver and excreted through the bile ducts.[17,18] After intravenous injection, bile ducts can be visualized under polarized light. Therefore, indocyanine green fluorescence cholangiography (ICG-FC) provides real-time imaging of the biliary system during surgery.[19] The use of ICG during LC may thus reduce perioperative complications and the length of hospital stay.

The primary endpoint of this investigation is the postoperative length of hospital stay (LOS), which serves as a highly objective surrogate marker for surgical efficiency, tissue trauma, and patient recovery.[20] Conceptually, by providing real-time fluorescent mapping of the extrahepatic biliary tract, ICG-FC reduces the cognitive and technical burden of identifying obscured anatomical landmarks.[21-22] This enhanced visualization is hypothesized to minimize unnecessary tissue dissection, thereby reducing intraoperative blood loss, lowering the risk of bile duct injury, and ultimately leading to a smoother postoperative recovery and a shortened LOS.[19,22]

In 2009, a study by Ishizawa et al. first demonstrated the potential benefit of ICG-assisted fluorescent cholangiography during LC.21 ICG-FC was shown to facilitate identification of key anatomical structures and detection of the biliary tract. A systematic review of 19 clinical studies by Serban et al. further confirmed the clinical value of ICG, concluding that ICG-FC is a promising tool for enhancing surgical safety during LC. The combination of ICG with white light has been shown to outperform white light alone in identifying extrahepatic biliary anatomy, thereby reducing the risk of bile duct injury and shortening postoperative hospital stay.[22] However, a study by She et al. reported no significant differences in the rate of conversion to open surgery or postoperative complications when using ICG-FC.[23]

In Thailand, studies evaluating the use of ICG during laparoscopic cholecystectomy, particularly in patients with difficult LC, remain limited. The researchers therefore anticipate that this study will provide valuable insight into the benefits



of ICG-assisted LC in difficult LC cases and contribute to data collection for future research development.

Materials and Methods

A cohort observational ambispective study was conducted in Buddhachinaraj Hospital in the period between 2020 and 2025. The study protocol was approved by the Institutional Review Board (IRB) of the Buddhachinaraj Hospital (No 039/2568). Data were obtained from patients who underwent elective LC between January 1, 2020, and December 31, 2025.

LC procedures were preoperatively categorized into easy, difficult, and very difficult levels based on the scoring system from the modified Randhawa's model 11-13 as described by Tongyoo and colleagues.[14,15]

Patients eligible for inclusion in this study were adults aged ≥ 18 years who were diagnosed with gallstone disease requiring laparoscopic cholecystectomy (LC) and were classified as difficult or very difficult LC according to the modified Randhawa's model. All participants underwent surgery at Buddhachinaraj Hospital and were scheduled for elective surgery. In this study, "elective surgery" strictly refers to scheduled procedures. Patients with a history of acute cholecystitis or acute cholangitis ("resolved acute" cases) were treated conservatively during their initial acute presentation and were subsequently scheduled for delayed or interval cholecystectomy once acute inflammatory symptoms had clinically resolved, in accordance with routine institutional practice. Eligible patients were required to have an American Society of Anesthesiologists (ASA) physical status classification of I–III, be able to communicate in Thai (listening, speaking, reading, and writing), and be capable of providing written informed consent prior to study participation. Patients were excluded if they declined participation or did not consent to data collection for the study. Additional exclusion criteria included a history of malignant hyperthermia or a first-degree relative with a history of malignant hyperthermia during anesthesia, as well as a documented allergy to indocyanine green (ICG).

In the non-ICG group, patients who underwent LC between January 1, 2020, and December 31, 2024, were identified through the hospital's electronic document system. Eligible patients in this historical cohort were selected using a convenience sampling approach, reviewing chronological records until the target sample size of 84 patients was met. Patient records and electronic medical records (EMR) were reviewed. Patient informed consent was waived because this was a retrospective study, and all data were used exclusively for research purposes.

In the ICG group, data were collected from patients scheduled for LC between January 1,



2025, and December 31, 2025. These patients were prospectively enrolled after obtaining approval from the institutional ethics review board. All participants provided written informed consent and were fully informed about the treatment they would receive. All procedures in both groups were performed by the same surgeon.

A pilot study was conducted using data from our center to estimate the difference in postoperative length of stay between the two operative techniques. The mean hospital stay was 4.2 days (±1.9) in the conventional LC group and 3.5 days (±1.2) in the ICG-FC LC group, with an observed mean difference of 0.7 days. Based on these values, a two-sample means test was applied for sample size estimation. Using a significance level of 0.05 (type I error or α), a power of 80%, and assuming equal allocation between the two groups, the required sample size was calculated to be 84 patients per arm, totaling 168 participants.

The data collection included patient characteristics, indication for surgery, physical examination result, radiological findings, and surgical outcomes. Baseline characteristics included age, sex, BMI, chronic comorbidities, ASA physical status, and history of previous abdominal surgery. Surgical outcomes including length of postoperative hospital stay, drain placement rate, conversion rate, intraoperative blood loss, operative time, and surgery-related complications were compared between the two groups. We followed the Strasberg classification of iatrogenic bile duct injury. No adverse reactions to ICG were documented. To prevent discharge bias due to the unblinded nature of the study, postoperative care and discharge criteria were strictly standardized across both the historical and prospective cohorts. While a formal Enhanced Recovery After Surgery (ERAS) pathway was not officially implemented, hospital discharge was determined based on standard clinical milestones, including adequate pain control with oral analgesics, tolerance of a solid diet, independent ambulation, and the absence of clinical complications.

Intraoperative fluorescence imaging with ICG

A dose of 1 mL (2.5 mg) of ICG manufactured by Taiyo Pharma Tech Co., Ltd, 25 mg/vial, diluted with 10 mL of sterile water was injected via peripheral vein by the anesthesiologist 15-30 minutes before the start of the operation. Although some literature suggests administration 4–24 hours preoperatively to optimize the target-to-background ratio by allowing hepatic parenchymal clearance, the immediate pre-procedural injection window (15–30 minutes) was adopted in this study. This timing was chosen because it aligns seamlessly with our hospital's elective surgical workflow, eliminating the logistical burden of an additional preoperative hospital visit for the patient. Furthermore, previous studies



have demonstrated that this timeframe provides adequate biliary visualization for safe dissection in Calot's triangle.[24,25] Laparoscopic fluorescence imaging system was used.

Statistical analysis

Statistical analysis was performed using STATA/MP version 16.1. Normally distributed continuous variables were described as mean ± standard deviation and analyzed with the student's *t*-test, whereas non-normally distributed continuous variables were described as medians with interquartile ranges and compared using the Mann-Whitney U test. Categorical variables were described as count and percentage and were analyzed with the Chi-square test or Fisher's exact test as appropriate. To account for potential confounding effects—particularly baseline imbalances between the two temporal cohorts—multivariable analyses were performed, adjusting for predetermined confounding variables including age, sex, BMI, and relevant comorbidities. The regression models were specifically chosen based on the type and distribution of the outcome variables. For non-normally distributed continuous outcomes (such as length of stay, intraoperative blood loss, and operative time), a quantile regression model (median regression) was utilized to directly estimate the adjusted median differences and their corresponding 95% confidence intervals. Conversely, for binary categorical outcomes (such as drain placement, conversion to open surgery, and surgery-related complications), a modified Poisson regression model with robust error variance was employed to estimate the adjusted risk ratio (aRR). The probability of less than 0.05 was used as a cut-off point for all significant tests.

Results

Patient characteristics

A total of 168 patients were included in the analysis, with 84 patients in each group. The baseline demographic and clinical characteristics of both groups were comparable.

The mean age of patients in the ICG-FC LC group was 53.4 ± 15.5 years, while the conventional LC group had a mean age of 56.4 ± 16.9 years (p = 0.224). Females constituted the majority in both groups (59.5% in the ICG-FC group vs. 69.0% in the conventional group; p = 0.260). The mean BMI was similar between the two cohorts (26.5 ± 4.51 vs. 26.4 ± 4.29 kg/m²; p = 0.878), and BMI subgroup distributions did not differ significantly. The indications for surgery did not differ significantly between groups. Resolved acute cholecystitis accounted for the largest



proportion in both groups (47.6% vs. 39.3%; p = 0.350). Both groups did not differ statistically in terms of previous abdominal surgery history, and radiological findings. Based on the modified Randhawa's scoring system, most patients in both groups fell into the "difficult" category (82.1% vs. 89.3%; p = 0.270), with the remainder classified as "very difficult" (Table 1). Regarding the safety profile of the intervention, all patients in the prospective cohort tolerated the ICG injection well. There were no documented adverse events, such as anaphylaxis, allergic reactions, or iodine cross-reactivity, confirming the excellent safety profile of the dye.

Table 1 Patient demographics

Character	ICG-FC LC (n = 84)	Conventional LC (n = 84)	*P* value
Age (years)[a]	53.4±15.5	56.4±16.9	0.224
≤ 50 years old	33 (39.3)	24 (28.6)	0.192
> 50 years old	51 (60.7)	60 (71.4)	
Sex			
Male	34 (40.5)	26 (31.0)	0.260
Female	50 (59.5)	58 (69.0)	
BMI (kg/m^2)[a]	26.5±4.51	26.4±4.29	0.878
< 25	21 (25.0)	27 (32.1)	0.629
25-27.5	24 (28.6)	22 (26.2)	
> 27.5	39 (46.4)	35 (41.7)	
Comorbidities			
Diabetes	18 (21.4)	22 (26.2)	0.587
Hypertension	40 (47.6)	34 (40.5)	0.437
ESRD	1 (1.2)	0 (0.0)	1.000
Cardiopathy[b]	6 (7.1)	6 (7.1)	1.000
Pulmonary disease[c]	0	5 (6.0)	0.059
Liver cirrhosis	2 (2.4)	2 (2.4)	1.000
ASA physical status			
ASA 1	4 (4.8)	11 (13.1)	0.165
ASA 2	50 (59.5)	43 (51.2)	
ASA 3	30 (35.7)	30 (35.7)	



Table 1 (cont.) Patient demographics

Character	ICG-FC LC (n = 84)	Conventional LC (n = 84)	*P* value
Indication for surgery[d]			
Symptomatic gallstone	20 (23.8)	17 (20.2)	0.710
Resolved acute cholecystitis	40 (47.6)	33 (39.3)	0.350
Resolved acute cholangitis	10 (11.9)	13 (15.5)	0.654
ERCP treated choledocholithiasis	14 (16.7)	14 (16.7)	1.000
Gallstone pancreatitis	9 (10.7)	16 (19.0)	0.193
Mirizzi syndrome	1 (1.2)	1 (1.2)	1.000
Previous procedure			
ERCP	29 (34.5)	37 (44.0)	0.341
Percutaneous cholecystostomy	2 (2.4)	6 (7.1)	
Previous abdominal surgery			
Lower abdominal surgery	35 (41.7)	25 (29.8)	0.197
Upper abdominal surgery	2 (2.4)	6 (7.1)	
Both	6 (7.1)	4 (4.8)	
Clinically palpable gallbladder	7 (8.3)	4 (4.8)	0.535
Radiological findings			
Wall thickness ≥ 4 mm	67 (79.8)	62 (73.8)	0.465
Pericholecystic collection	13 (15.5)	13 (15.5)	1.000
Impacted stone	33 (39.3)	25 (29.8)	0.256
Contracted gallbladder	23 (27.4)	20 (23.8)	0.724
Modified Randhawa's score			
Difficult (6-10)	69 (82.1)	75 (89.3)	0.270
Very difficult (11-15)	15 (17.9)	9 (10.7)	

NOTE: Values in parenthesis are percentage, unless indicated otherwise.
ICG-FC, indocyanine green fluorescence cholangiography; LC, laparoscopic cholecystectomy; BMI, body mass index; ESRD, end-stage renal disease; ASA, American Society of Anesthesiologists classification physical status; SD, standard deviation.
[a] Values are mean ± SD.
[b] Cardiopathy, coronary artery disease, valvular heart disease, atrial fibrillation
[c] Pulmonary disease, asthma, chronic obstructive pulmonary disease
[d] Patients may have had more than one indication

Surgical outcomes

Overall surgical outcomes

Overall surgical outcomes are summarized in Table 2. Patients undergoing ICG-FC LC experienced a significantly shorter postoperative length of stay compared with those undergoing conventional LC (median 1.4 vs. 2.1 days; adjusted median difference −0.62 days, 95% CI −1.23 to −0.01; p = 0.047). Intraoperative blood loss was significantly lower in the ICG-FC LC group, with an adjusted median difference of −5.7 mL (95% CI −6.9 to −4.5; $p < 0.001$). Operative time was also reduced, with an adjusted median difference of −14.4 minutes (95% CI −17.6 to −11.2; $p < 0.001$). Among cases requiring conversion to open surgery, the time to conversion was shorter in the ICG-FC LC group, with an adjusted median difference of −12.6 minutes (95% CI −20.9 to −4.4; p = 0.003).

Regarding categorical outcomes, drain placement rates were similar between groups (35.0% vs. 42.7%; adjusted risk ratio [aRR] 0.82, 95% CI 0.55–1.21; p = 0.303). Conversion to open cholecystectomy and partial cholecystectomy rates were also comparable, with adjusted ratios close to unity and no statistically significant differences.

Postoperative complications were infrequent and did not differ significantly between groups. Biliary complications, including bile duct injury or bile leakage, were rare, occurring in 1.2% of patients in both groups (aRR 1.00, 95% CI 0.97–1.03; p = 0.951). No major bile duct transections or injuries requiring reconstructive biliary surgery were identified. All biliary-related events were managed successfully with conservative treatment or minor interventions, such as ERCP with plastic stent placement, without procedure-related mortality. Wound infection rates were low (2.4% in the ICG-FC LC group vs. 3.6% in the conventional LC group; aRR 0.98, 95% CI 0.93–1.04; p = 0.591) and were predominantly superficial, managed conservatively without reoperation. Other postoperative complications—such as adjacent organ injury (small bowel or transverse colon), early postoperative bowel obstruction, and cholangitis—were uncommon and similarly distributed between groups. No surgery-related mortality was observed.



Table 2 Overall surgical outcomes

Outcomes	ICG-FC LC (n = 84)	Conventional LC (n = 84)	Adjusted Median Difference [95% CI][a]	Adjusted Risk Ratio [95% CI][b]	*p*-value
Continuous Outcomes					
LOS (days) [IQR]	1.4 [1.2, 1.8]	2.1 [1.8, 2.5]	-0.62 [-1.23, -0.01]	-	0.047
Intraoperative blood loss (mL) [IQR]	18.3 [17.5, 19.1]	27.0 [26.0, 28.1]	-5.7 [-6.9, -4.5]	-	< 0.001
Operative time (min) [IQR]	99.0 [96.9, 101.1]	114.0 [111.7, 116.3]	-14.4 [-17.6, -11.2]	-	< 0.001
Time to conversion (min) [IQR]	15.9 [12.4, 19.5]	25.1 [20.6, 29.5]	-12.6 [-20.9, -4.4]	-	0.003
Categorical Outcomes (%)					
Drain placement	35.0	42.7	-	0.82 [0.55, 1.21]	0.303
Conversion to OC	6.0	6.0	-	1.03 [0.96, 1.10]	0.438
Partial cholecystectomy	13.1	13.1	-	1.03 [0.93, 1.14]	0.550
Surgical-related complications					
BDI or Bile leakage	1.2	1.2	-	1.00 [0.97, 1.03]	0.951
Wound infection	2.4	3.6	-	0.98 [0.93, 1.04]	0.591
Other[c]	1.2	2.4	-	0.99 [0.95, 1.04]	0.940

95% CI, 95% confidence interval; ICG-FC, indocyanine green fluorescence cholangiography; LC, laparoscopic cholecystectomy; LOS, length of stay; OC, open cholecystectomy; BDI, bile duct injury; IQR, interquartile range.

[a] Calculated using a quantile regression model adjusted for age, sex, BMI, and comorbidities.

[b] Calculated using a modified Poisson regression model with robust error variance adjusted for age, sex, BMI, and comorbidities.

[c] Other: adjacent organ injury (small bowel, transverse colon, liver segment 4), early post-operative bowel obstruction, cholangitis.

Outcomes stratified by case difficulty

To facilitate direct comparison of surgical outcomes across different levels of surgical complexity, the results for both 'difficult' and 'very difficult' subgroups have been merged into a single comprehensive presentation (Table 3).

Among patients classified as having difficult LC, ICG-FC LC was associated with a significantly shorter postoperative length of stay (1.3 vs. 1.9 days; adjusted median difference −0.6 days, 95% CI −0.9 to −0.3; $p < 0.001$). Intraoperative blood loss was also markedly reduced in the ICG-FC



LC group (9.9 vs. 25.1 mL; adjusted median difference −11.3 mL, 95% CI −12.6 to −10.0; $p < 0.001$). No statistically significant differences were observed in operative time, drain placement, conversion to open surgery, time to conversion, or partial cholecystectomy rates. Biliary-related complications were not statistically significantly different between groups. Other surgical-related complications were rare (1.4% vs. 2.7%; $p = 0.906$).

In very difficult LC cases, postoperative length of stay did not differ significantly between groups (2.0 vs. 3.4 days; $p = 0.125$). Most perioperative outcomes, including operative time, drain placement, conversion to open surgery, time to conversion, and partial cholecystectomy rates, were also comparable after adjustment. Conversely, the quantile regression model revealed that intraoperative blood loss was significantly higher in the ICG-FC LC group compared with the conventional LC group (70.3 vs. 31.6 mL; $p = 0.008$), yielding an adjusted median difference of 36.4 mL (95% CI 9.8 to 63.0; $p = 0.008$). Postoperative complication rates did not differ significantly between groups. One case in the ICG-FC LC group developed a biliary leak from the gallbladder remnant on postoperative day 1, which was successfully managed with ERCP and plastic stent placement. No surgery-related mortality was observed in this subgroup.

Table 3 Surgical outcomes stratified by case difficulty (Difficult vs. Very Difficult LC)

Outcomes	Difficult LC (n = 144)				Very Difficult LC (n = 24)			
	ICG (n=69)	Control (n = 75)	Adj. Estimate [95% CI]	*p*-value	ICG (n = 15)	Control (n = 9)	Adj. Estimate [95% CI]	*p*-value
Continuous Outcomes[a]								
LOS (days)	1.3	1.9	-0.6 [-0.9, -0.3]	< 0.001	2.0	3.4	-1.3 [-3.0, 0.4]	0.125
Blood loss (mL)	9.9	25.1	-11.3 [-12.6, -10.0]	< 0.001	70.3	31.6	36.4 [9.8, 63.0]	0.008
Operative time (min)	94.3	103.7	-8.1 [-18.9, 2.8]	0.143	130.7	139.6	-23.6 [-64.1, 16.9]	0.232
Time to conversion (min)	10.0	28.8	-18.8 [-51.5, 14.0]	0.261	16.3	15.0	1.2 [-16.2, 17.7]	0.881
Categorical Outcomes (%)[b]								
Drain placement	30.4	38.7	0.79 [0.45, 1.38]	0.560	53.3	66.7	0.80 [0.35, 1.82]	0.928



Table 3 (cont.) Surgical outcomes stratified by case difficulty (Difficult vs. Very Difficult LC)

Outcomes	Difficult LC (n = 144)				Very Difficult LC (n = 24)			
	ICG (n=69)	Control (n=75)	Adj. Estimate [95% CI]	*p*-value	ICG (n=15)	Control (n=9)	Adj. Estimate [95% CI]	*p*-value
Conversion to OC	1.4	5.3	0.98 [0.93, 1.04]	0.549	26.7	11.1	1.19 [0.79, 1.80]	0.392
Partial cholecystectomy	8.7	10.7	1.00 [0.91, 1.11]	0.965	33.3	33.3	1.19 [0.76, 1.86]	0.431
Surgical complications								
BDI or Bile leakage	0	1.3	0.98 [0.95, 1.01]	0.291	6.7	0	1.12 [0.92, 1.36]	0.252
Wound infection	0	2.7	0.97 [0.93, 1.01]	0.169	13.3	11.1	1.04 [0.71, 1.52]	0.815
Other[c]	1.4	2.7	0.99 [0.95, 1.04]	0.906	0	0	-	-

95% CI, 95% confidence interval; ICG, indocyanine green; Control, conventional laparoscopic cholecystectomy; LOS, length of stay; OC, open cholecystectomy; BDI, bile duct injury.

[a] Adjusted Estimates for continuous outcomes represent the Adjusted Median Difference calculated using a quantile regression model (adjusted for age, sex, BMI, and comorbidities).

[b] Adjusted Estimates for categorical outcomes represent the Adjusted Risk Ratio calculated using a modified Poisson regression model with robust error variance (adjusted for age, sex, BMI, and comorbidities).

[c] Other: adjacent organ injury, early post-operative bowel obstruction, cholangitis.

Discussion

This study demonstrates that indocyanine green fluorescence–guided laparoscopic cholecystectomy (ICG-FC LC) provides measurable perioperative benefits compared with conventional laparoscopic cholecystectomy, particularly in patients with difficult LC. After adjustment for baseline characteristics and comorbidities, the use of ICG fluorescence guidance was associated with a shorter postoperative length of stay and reduced intraoperative blood loss in the overall cohort. These findings suggest that improved intraoperative visualization of biliary anatomy may facilitate safer and more efficient dissection, thereby accelerating postoperative recovery. Consistent with our conceptual framework, this enhanced visualization minimizes inadvertent tissue trauma and decreases blood loss, which directly translates to the shortened hospital stay observed in our study.



The benefits of ICG-FC LC were most pronounced in patients with difficult LC. In this subgroup, ICG-FC LC significantly shortened postoperative length of stay and reduced blood loss without increasing operative time, conversion to open surgery, or the need for partial cholecystectomy. These results are clinically relevant, as difficult LC is commonly associated with prolonged hospitalization and increased operative complexity. The findings support the role of ICG fluorescence cholangiography as an adjunctive tool to enhance surgical efficiency in challenging cases where anatomical landmarks are obscured but the tissue remains amenable to near-infrared penetration.

With regard to biliary safety, bile duct injury and bile leakage were rare events in this study. No biliary injuries occurred in the ICG-FC LC group among patients with difficult LC, whereas one minor bile duct injury (Strasberg type A) was observed in the conventional LC group and was successfully managed intraoperatively. However, after adjustment, no statistically significant difference in biliary-related complications was detected between groups likely due to the rarity of these events. This suggests that while ICG-FC LC may aid intraoperative decision-making, its protective effect against bile duct injury cannot be conclusively established based on the present data. Importantly, the administration of ICG was completely safe, with no incidents of anaphylaxis or iodine cross-reactivity observed in our cohort, which validates the excellent safety profile of this dye.

In very difficult LC cases, postoperative length of stay and most perioperative outcomes were comparable between groups. Importantly, postoperative complication rates, including biliary-related events, were similar between groups, and no surgery-related mortality was observed. However, a critical clinical paradox was observed regarding intraoperative blood loss, which was significantly higher in the ICG-FC LC group (70.3 vs. 31.6 mL). This phenomenon can be attributed to the physical limitations of near-infrared (NIR) fluorescence technology. NIR light typically penetrates only 5 to 10 millimeters of tissue. In conditions characterized by severe subserosal edema, dense retrocholecystic fibrosis, or scleroatrophic gallbladders, the near-infrared signal is severely attenuated or completely obscured. Consequently, surgeons may perform more extensive and meticulous dissections in an attempt to identify the non-visualized fluorescent structures, which, combined with the inherent fragility of chronically inflamed tissues, paradoxically leads to increased bleeding. The wide confidence intervals in this subgroup highlight the limited sample size and underscore the need for cautious interpretation.

Several major limitations should be acknowledged. First and foremost, the study's



ambispective design introduces a profound chronological and learning curve bias. Because the conventional group was treated historically (2020–2024) while the ICG group was treated prospectively (2025) by a single surgeon, the observed reductions in operative time and blood loss may partially reflect the natural progression of the surgeon's technical competence and familiarity with complex cases over a 5-year period, rather than the sole effect of the ICG intervention. Second, while the modified Randhawa scoring system provided institutional utility for stratifying difficulty, it currently lacks widespread external validation in multicenter settings compared to standard tools like the Tokyo Guidelines. Third, although a Poisson regression model was utilized to adjust for known baseline variables, there may still be unmeasured confounding factors, such as minor variations in anesthetic care. Finally, the sample size—particularly in the very difficult LC subgroup—limits statistical power for rare outcomes such as bile duct injury. Despite these limitations, the consistent findings across adjusted analyses strengthen the validity of the observed associations in selected difficult cases.

Conclusion

ICG fluorescence–guided laparoscopic cholecystectomy was associated with a shorter postoperative length of stay and reduced intraoperative blood loss compared with conventional laparoscopic cholecystectomy, particularly in patients with difficult LC, while maintaining comparable perioperative and postoperative safety outcomes. However, these technological benefits appear to reach a physical limitation in "very difficult" cases with dense fibrosis or severe edema, where ICG-FC may paradoxically be associated with increased blood loss due to obscured signals and subsequent extensive dissection. Although no significant reduction in biliary-related complications was demonstrated after adjustment, ICG fluorescence cholangiography appeared to be generally safe in selected difficult LC cases. These findings support the selective use of ICG fluorescence guidance in difficult laparoscopic cholecystectomy to improve surgical efficiency and postoperative recovery, while keeping in mind the necessity of surgical experience in overcoming its physical limitations.

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