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RESEARCH

Low-dose indocyanine green fluorescence cholangiography in laparoscopic cholecystectomy: visualization performance across validated risk scores

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Abstract

Background Laparoscopic cholecystectomy(LC) is the standard treatment for gallbladder disease. However, complex cases may require conversion to open surgery. Indocyanine green near-infrared fluorescence cholangiography(ICG NIRF-C) enhances biliary visualization, potentially reducing conversion rates, surgical time and complications.This study evaluates ICG's role in improving LC outcomes using five predictive risk scores.

Study design Forty-four LC patients received a single 0.25 mg intravenous ICG dose during anesthesia induction. Data collected included demographics, biliary visualization before and after dissection, complications, operative time and risk scores.

Results ICG fluorescence improved biliary visualization: common bile duct(CBD) was identified in 29% of cases before and 100% after dissection. Despite 61.4% of patients having a CLOC score > 6 and 43.2% a G10 score ≥ 3 no conversions occurred. Only 7% of cases exceeded 90 min (p = 0.03).

Conclusion ICG NIRF-C enhanced biliary visualization and, in this cohort, was associated with absence of conversions and favorable operative-time profiles across risk strata. These findings are observational and hypothesis-generating, supporting further comparative evaluation, particularly in complex cases.

Introduction

Since its introduction in the late 1980 s, laparoscopic cholecystectomy (LC) has become the gold standard for treating gallbladder disease [1–6]. This minimally invasive technique offers numerous advantages, such as faster recovery, reduced postoperative pain, and shorter hospital stays [1, 7–9]. Additionally, ambulatory LC has gained recognition as a safe and effective procedure, enabling faster recovery in a home setting [8, 9]. However, conversion to open surgery remains a challenging necessity in certain cases due to severe inflammation, anatomical variations, or extensive adhesions. These factors increase the difficulty of identifying biliary anatomy, leading to higher morbidity, longer hospitalizations, and significantly increased costs [2, 4, 7, 9]. Notably, the primary cause of bile duct injury (BDI) in up to 97% of cases is misinterpretation of biliary structures [5, 6]. Intraoperative cholangiography (IOC) has long been used as

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a standard technique to delineate biliary anatomy and reduce the risk of bile duct injury. However, IOC requires cystic duct cannulation and exposes patients and staff to radiation, which limits its universal adoption [9]. In this context, contrast agents such as indocyanine green (ICG) have emerged as a promising alternative to enhance intraoperative visualization of the biliary tree, potentially reducing complications, shortening surgical times, and preventing conversions to open surgery [10–12].

In this study, we aimed to evaluate the impact of indocyanine green near-infrared fluorescence cholangiography (ICG NIRF-C) in laparoscopic cholecystectomy (LC), particularly in high-risk cases, by analyzing its effect on biliary structure visualization, conversion to open surgery, operative time, and potential implications for ambulatory surgery. To support these claims, we examine five predictive scoring systems: CLOC, G10, CAAD, the Nassar Score (2019), and the Surgical Time Score (CholeS Study Group).

Materials and methods

Trial design and patients

This was a prospective descriptive study. Ethical clearance for the study was granted by the institutional review board, designated as CI-344-19. Patients underwent surgery between January 2019 and January 2020. Sample size was prospectively calculated for the primary endpoint (biliary visualization). Based on a one-sample non-inferiority test (p_0=0.85, $\Delta = 0.13$, $\alpha = 0.05$ one-sided, power 80%), 40 patients were required; 44 were included to account for attrition. All surgeries were performed by the same surgical team, thus neutralizing any bias with respect to observation of the biliary anatomy while using ICG NIRF-C. Those patients with a prior history of symptomatic cholelithiasis such as biliary colic, acute or chronic cholecystitis, choledocholithiasis, pancreatitis or gallbladder polyps were enrolled in the study to undergo LC with NIR-ICG fluorescence imaging. Other inclusion criteria were age $\geq$ 18 years old, normal liver and kidney function, no allergies to ICG or iodine, ability to understand and follow study procedures and having provided signed consent. The exclusion criteria were age < 18 years old, liver or kidney dysfunction, known history of cholangitis or prior common bile duct injury, allergy to ICG or iodine, pregnancy or breast-feeding and inability to understand and follow study procedures.

None of the patients was taking medication interfering with hepatic ICG uptake.

The patient withdrawal criteria were withdrawal of informed consent or lost to follow-up.

Patient data were collected at enrolment, during surgery, immediately after surgery and up to 90 days postoperatively.

Outcomes measures

The data recorded included age, gender, diabetes mellitus, hypertension, dyslipidaemia, body mass index (BMI), American Society of Anaesthesiologists (ASA) physical status classification, surgical indication, intraoperative complications, hepatic hyperluminescence, visualization of biliary structures such as the cystic duct (CD), the common bile duct (CBD) and the cystic duct–bile duct junction (CDBDJ) before and after dissection of Calot's triangle, conversion to open surgery, postoperative complications graded according to the Clavien–Dindo classification [24], BDI described according to Strasberg classification [25], hospital stay and readmission.

In our study, we have also used the Nassar classification [17] to perform a visual intraoperative assessment of the surgical difficulty at the beginning of each cholecystectomy given that it is easy to use and reproducible and reflects the tendency to suffer from BDIs as well as prolonged surgical times and conversion to open surgery. The Nassar scale grades operative findings [17] from the gallbladder, cystic pedicle and associated adhesions. In grade 1, the gallbladder is floppy and non-adherent, the cystic pedicle is thin and clear, and the adhesions are simple up to the neck/Hartmann's pouch. In grade 2, the gallbladder can be packed with stones, the cystic pedicle is fat laden, and adhesions are simple up to the body. In grade 3, the gallbladder can have a deep fossa, acute cholecystitis and fibrosis, and Hartmann's pouch is adherent/impacted to CBD. The cystic pedicle can have abnormal anatomy, or the cystic duct is short, dilated or obscured. Adhesions are dense up to the fundus or involving hepatic flexure or duodenum. In grade 4, the gallbladder is completely obscured or can have empyema or gangrene. The cystic pedicle is impossible to clarify, and adhesions are dense with fibrosis, wrapping the gallbladder. The duodenum and/or hepatic flexure are difficult to separate.

On the other hand, when we analyse the variable "gallbladder inflammation", it corresponds to the pathological anatomy of the surgical specimen and is classified as absence of inflammation, acute inflammation, or chronic inflammation.

Surgical and fluorescence cholangiography techniques

ICG is a fluorophore that, when administered intravenously, binds to plasma proteins and is primarily eliminated by the liver enhancing the perception of biliary anatomy [10–28]. A unique dose of 0.25 mg of ICG dye was administered intravenously 15 min before the surgery during the anaesthesia induction. After placing ports, the scope was introduced into the abdominal cavity. We then exposed the gallbladder in order to visualize Calot’s triangle and recorded the exact moment when Calot’s triangle first became visible by ICG NIRF-C imaging before performing dissection. We confirmed the absence of aberrant bile ducts and then bluntly dissected Calot’s triangle after achieving the “critical view of safety” described by Strasberg and isolating the cystic duct and cystic artery with ICG NIRF-C in overlay mode. The cystic duct and cystic artery were clipped and divided after confirming the CDBDJ using fluorescence cholangiography. We then dissected the gallbladder from the liver bed. Upon completion of all laparoscopic procedures, we performed NIRF-C again to examine the cystic duct stump and confirm the absence of any bile leakage. Finally, the gallbladder was removed from the abdomen using a retrieval bag.

Laparoscopic equipment

We used the VISERA ELITE II Surgical Endoscope System (Olympus Corporation, Shinjuku, Tokyo, Japan) for NIR/ICG imaging with a 30° forward oblique laparoscope. NIR images were obtained by combining an infrared light source and infrared telescope with the video system centre, camera head and monitor used for white light (WL) images. Images can be switched between WL and NIR light by pushing a button conveniently located on the camera head. The OTV-S300 video system centre uses an LED light source instead of a xenon lamp. During LC, alternating exposure to WL to NIR light sources can be used to identify biliary structures before, during and after dissection. In overlay mode, the regular WL image is combined with the NIR/ICG data to generate an overlay image. In our study, we performed all surgeries in overlay mode in order to identify each ICG stained biliary structure while dissecting Calot’s triangle.

Predictive scoring systems

We have also investigated the relationship between ICG NIRF-C during LC and five surgical risk assessment systems: CLOC [27], G10 [26], Nassar Score (2019) [30], CAAD [28] and the Surgical Time Score [29] (from the CholeS Study Group). These scoring systems were chosen because they provide valuable insights into key surgical challenges, such as predicting conversion to open surgery, assessing surgical complexity, and estimating operative time.

The CLOC score is a validated preoperative risk assessment tool designed to predict the likelihood of conversion from laparoscopic to open cholecystectomy [27]. As described in this study, we have also stratified patients as **higher risk of conversion** if they had a **CLOC score > 6** [27].

The G10 score is an intraoperative gallbladder scoring system prospectively evaluated to predict surgical outcomes, particularly the feasibility of completing the operation laparoscopically [26]. This scoring system was developed in a multicenter study led by the World Society of Emergency Surgery [26]. Gallbladder surgery was considered easy if the G10 score < 2, moderate (2 ≦ 4), difficult (5 ≦ 7) and extreme (8 ≦ 10) [26]. The optimal cut-off point of 0.067 (score of 3) was identified in G10 and conversion to open cholecystectomy occurred in 33% of patients with G10 scores of ≥ 5 [26]. We categorized our patients at **higher risk of conversion to open surgery** with G10 scores meeting the following thresholds: **G10 ≥ 3** (moderate or higher difficulty) and **G10 ≥ 5** (difficult or extreme cases).

The **Nassar scoring system (2019)** is a predictive tool for assessing surgical difficulty in laparoscopic cholecystectomy and estimating the likelihood of conversion to open surgery based on operative findings [30]. It classifies cases into three risk levels—low (0–2 points), intermediate (3–4 points), and high (≥ 5 points)—to help anticipate surgical complexity, prolonged operative times, and potential complications [30]. In our study, patients were stratified accordingly into these three categories.

The CAAD score is a validated system for predicting the success of day-case cholecystectomy operations) [28]. It was developed using data from a prospectively collected dataset of cholecystectomy patients from 166 UK and Irish hospitals (CholeS study)) [28]. This score is based on 10 preoperative factors, including patient demographics (age and gender), comorbidities (ASA score), history of previous hospital admissions for gallstone-related disease, primary indication for surgery (such as biliary colic, cholecystitis, or choledocholithiasis), preoperative imaging findings (thickened gallbladder wall or dilated common bile duct), and the type of preoperative investigations performed (radiological or endoscopic) [28]. Patients were identified as having a greater risk of unsuccessful day-case cholecystectomy if their **CAAD score > 5** [28]. By incorporating these variables, the CAAD score provides an objective tool for preoperative patient selection, optimizing surgical planning and resource allocation.

Finally, the **Surgical Time Score** was developed to predict whether **a surgery will exceed 90 min**, helping to optimize operating room scheduling [29]. This score is based on 10 preoperative factors and categorizes patients into low (0–3 points), intermediate (4–7 points), or high risk (8 points or more) for prolonged operative time [29]. It has been validated and shown to improve efficiency in surgical planning [29]. In our study, the surgical times were also divided into three categories: less than 45 min, between 45 and 90 min, and more than 90 min.

Statistical analysis

Our sample size was prospectively justified for the primary visualization endpoint. Based on a one-sample non-inferiority test ($p_0 = 0.85$, $\Delta = 0.13$, $\alpha = 0.05$ one-sided, power 80%), 40 patients were required; we included 44 to account for attrition. Normality tests and graphs were used to determine whether variables followed a normal distribution. Data are presented as mean ± standard deviation (SD) for continuous variables, and those a non-normal distribution are expressed as median values and interquartile ranges. We used Student's *t* test or the Wilcoxon test for paired samples for the quantitative variables. The Chi-square test and McNemar's test were used for qualitative variables. Pearson's correlation coefficient was used to determine the linear dependence between two quantitative variables. ANOVA test was used to compare continuous variable means of two or more groups. Linear regression analysis was also performed to assess the association of continuous variables. A *p* value of less than 0.05 was considered statistically significant. Statistical analyses were carried out with SPSS software 23.0 (SPSS Inc., Chicago, IL, USA).

Results

Forty-four patients (16 females (36%) and 28 males (64%)) were eligible for elective LC and included in our study. The mean age was 57 ± 15 years. According to ASA score, 9 patients (20%) were ASA I, 24 (55%) were ASA II, and 11 (25%) were ASA III. Their mean BMI was 28 ± 5 kg/m2. The mean operation time was 45 ± 15 min. The indications for surgery were 13 cases of symptomatic cholelithiasis (30%), 7 of choledocholithiasis (treated with preoperative endoscopic retrograde cholangiopancreatography) (16%), 12 of previous cholecystitis (27%) and 12 of lithiasic pancreatitis (27%). Twenty patients (45%) did not have gallbladder inflammation, 22 (50%) had chronic inflammation, and only 2 (5%) had acute inflammation. When classifying patients according to their Nassar grade, 20 (45%) were grade 1, 13 (29%) were grade 2, 8 (18%) were grade 3, and only 3 patients (7%) were grade 4.

While the proportion of acute cases was low, complexity was significant according to objective scores. The cohort included substantial predicted difficulty according to validated risk scores: 61.4% had CLOC > 6, 43.2% had G10 ≥ 3 (18.2% G10 ≥ 5), 45.5% were high risk by Nassar-2019, 63.6% had CAAD > 5, and 25% were grade 3–4 intraoperatively by the Nassar classification. These findings confirm the cohort was not restricted to 'easy' cases.

ICG NIRF-C was performed during LC in all 44 cases. No allergic reactions to ICG were reported. There were no BDIs and no conversions to laparotomy. The postoperative course was free of complications in all cases. The mean postoperative hospital stay was 28 ± 4 h. No hospital readmissions were recorded. All other patient characteristics, intraoperative data and postoperative outcomes are reported in Table 1.

Ability of fluorescence cholangiography to delineate the bile duct anatomy

The CD or the CDBDJ could not be identified via fluorescence cholangiography in any of the patients before dissection of Calot's triangle, whereas the CBD was detected using ICG NIRF-C in 13 patients (29%) before dissection of Calot's triangle (Table 2).

After dissecting Calot's triangle (at average time of 25 min after starting surgery), ICG NIRF-C identified the CD and the CDBDJ in 31 (71%) and 37 (84%) patients, respectively. The CBD was detected in all 44 patients with ICG NIRF-C after dissection of Calot's triangles. Statistically significant differences in the identification of the three bile structures using ICG NIRF-C were found before and after the dissection of Calot's triangle (Table 2). No accessory bile ducts were identified in any of the LC interventions during ICG NIRF-C. No hepatic hyperluminescence was observed in any of the patients at an ICG dose of 0.25 mg.

Clinical factors affecting the ability of fluorescence cholangiography to delineate the bile duct anatomy

Table 3 summarizes the effects of clinical factors such as obesity and the degree of inflammation on the ability of ICG NIRF-C to delineate bile duct anatomy before and after dissecting Calot's triangle.

We observed statistically significant differences in the visualization of the CBD using ICG NIRF-C before dissecting Calot's triangle in patients with a Nassar grade < 3 ($p = 0.013$) and no gallbladder inflammation ($p = 0.001$). In this manner, ICG NIRF-C could detect the CBD in 13 patients (39%) with a Nassar grade < 3 before dissection of Calot's triangle and in 20 patients (65%) without gallbladder inflammation. There were no differences with respect to these clinical factors in the visualization of the rest of the biliary structures when using ICG NIRF-C before and after dissection of Calot's triangle except for the post- dissection visualization of the CDBDJ in patients with no gallbladder inflammation ($p = 0.008$) (Table 3).

Relationship between CLOC, G10, CAAD, Nassar 2019 Scores and and Surgical Time Score (CholeS Study Group) and the Duration of Surgery

Table 1 Patient characteristics, intraoperative data and postoperative outcomes

Total number of patients	44
Age (years) a	57±15
Gender	16 F (36%); 28 M (64%)
ASA score	
ASA I	9 (20%)
ASA II	24 (55%)
ASA III	11 (25%)
BMI (kg/m^2) a	28±5
- BMI<30	31 (70%)
- BMI≥30	13 (30%)
Smoker	17 (39%)
Diabetes mellitus	7 (16%)
Arterial hypertension	23 (52%)
Hypercholesterolaemia	18 (41%)
Hypertriglyceridaemia	6 (14%)
Surgical indication	
Symptomatic cholelithiasis	13 (30%)
Choledocholithiasis	7 (16%)
Cholecystitis	12 (27%)
Lithiasic pancreatitis	12 (27%)
Gallbladder inflammation	
No inflammation	20 (45%)
Acute inflammation	2 (5%)
Chronic inflammation	22 (50%)
Nassar Grade	
Grade 1	20 (45%)
Grade 2	13 (29%)
Grade 3	8 (18%)
Grade 4	3 (7%)
Hepatic hyperluminescence effect	0 (0%)
Operation time (min) [b]	45±15
CLOC score>6 27 (61,4%)	
G10 score≥3	19 (43,2%)
G10 score≥5	8 (18,2%)
CAAD score>5	28 (63,6%)
Surgical Time Score (CholeS Study Group)	
Low score	9 (20.4%)
Intermediate score	32 (72.7%)
High score	3 (6.8%)
Nassar Score 2019	
Low score	11 (25%)
Intermediate score	13 (29.5%)
High score	20 (45.5%)
Perioperative complications	0 (0%)
Mean hospital stay (hours) [b]	28±4
Readmissions	0 (0%)

Categorical values are presented as percentages. [a] Normally distributed variables are expressed as mean and standard deviation (SD). [b] Non normally distributed variables are expressed as median and interquartile range

ASA; American Society of Anaesthesiologists, *BMI*; body mass index; *VAS*; visual analogue scale

Table 2 Identification of biliary structures with NIR light

	Before dissection of Calot's triangle (*n*=44)	After dissection of Calot's triangle (*n*=44)	*p*
CD, n (%)	0 (0%)	31 (71%)	*0.001*
CBD, n (%)	13 (29%)	44 (100%)	*0.001*
CDBDJ, n (%)	0 (0%)	37 (84%)	*0.001*

McNemar test was used for qualitative variables. p-value<0.05 is considered statistically significant

NIR; near infrared, *CD*; cystic duct, *CBD*; common bile duct, *CDBDJ*; cystic duct-bile duct junction

Table 4 summarizes the relationship between CLOC, G10, CAAD and Nassar 2019 Scores and surgical times. Statistically significant differences were only observed in patients with G10 score≥3 (p=0.01) and G10 score≥5 (p=0.03).

In this manner, 14 patients (56%) with G10<3 had a surgical time<45 min; 11 (44%) had a surgical time between 45 and 90 min and none of the patients with G10<3 had a surgical time>90 min. Four patients (21%) with G10≥3 had a surgical time<45 min; 12 (63%) had a surgical time between 45 and 90 min and 3 (16%) had a surgical time>90 min.

On the other hand, 17 patients (47%) with G10<5 had a surgical time<45 min; 18 (50%) had a surgical time between 45 and 90 min and 1 patient (2.8%) had a surgical time>90 min. One patient (12.5%) with G10≥5 had a surgical time<45 min; 5 (62.5%) had a surgical time between 45 and 90 min and 2 (7%) had a surgical time>90 min.

In our study, there were only 3 patients with a surgical intervention lasting more than 90 min, which corresponded to an intermediate score according to the Surgical Time Score (CholeS Study Group).

Relationship between the ability of fluorescence cholangiography to delineate the bile duct anatomy before and after dissection of Calot's triangle and CLOC, G10, CAAD, Nassar 2019 Risk Scores and Surgical Time Score (CholeS Study Group)

Twenty-seven patients (61,4%) had a CLOC score>6, 19 patients (43,2%) had G10 score≥3, 8 patients (18,2%) had G10 score≥5 and 28 (63,6%) had a CAAD score>5. Regarding surgical Time Score (CholeS Study Group), nine patients (20.4%) had a low score, 32 (72.7%) had a intermediate score and 3 (6.8%) had a high score. Finally, eleven patients (25%) had a low Nassar Score 2019, 13 (29.5%) had a intermediate score and 20 (45.5%) had a high score.

Table 3 Clinical factors that May affect the ability of ICG NIRF-C to delineate biliary structures before and after dissection of calot's triangle, $n=44$

	Before dissection of Calot's triangle						After dissection of Calot's triangle					
	CD, n (%)	*p*	CBD, n (%)	*p*	CDBDJ, n (%)	*p*	CD, n (%)	*p*	CBD, n (%)	*p*	CDBDJ, n (%)	*p*
BMI, n (%)												
<30, 32 (70%)	0 (0%)	-	12 (37.5%)	*0.06*	0 (0%)	-	21 (65%)	*0.25*	32 (100%)	-	27 (84%)	*0.93*
≥30, 12 (30%)	0 (0%)		1 (8.3%)		0 (0%)		10 (83%)		12 (100%)		10 (83%)	
Nassar Grade, n (%)												
<3, 33 (75%)	0 (0%)	-	13 (39%)	*0.013*	0 (0%)	-	23 (70%)	*0.85*	33 (100%)	-	29 (88%)	*0.23*
≥3, 11 (25%)	0 (0%)		0 (0%)		0 (0%)		8 (73%)		11 (100%)		8 (73%)	
Gallbladder inflammation, n (%)												
No inflammation, 20 (45%)	0 (0%)	-	13 (65%)	*0.001*	0 (0%)	-	14 (70%)	*0.95*	20 (100%)	-	20 (100%)	*0.008*
Inflammation, 24 (55%)	0 (0%)		0 (0%)		0 (0%)		17 (71%)		24 (100%)		17 (71%)	

McNemar test was used for qualitative variables. *p*-value<0.05 is considered statistically significant

Table 4 Relationship between CLOC, G10, CAAD risk scores, surgical time score (CholeS study Group) and surgical time; $n=44$

Surgical Time				
	<45 min, n (%)	45–90 min, n (%)	>90 min, n (%)	*p*
CLOC, n (%)				
≦6, 17 (38.6%)	8 (47%)	7 (41%)	2 (12%)	*0.38*
>6, 27 (61.4%)	10 (37%)	16 (59%)	1 (4%)	
G10, *n* (%)				
<3, 25 (56.8%)	14 (56%)	11 (44%)	0 (0%)	*0.01*
≥3, 19 (43.2%)	4 (21%)	12 (63%)	3 (16%)	
<5, 36 (81.8%)	17 (47%)	18 (50%)	1 (2,8%)	*0.03*
≥5, 8 (18.2%)	1 (12,5%)	5 (62,5%)	2 (25%)	
CAAD, *n* (%)				
≦5, 16 (36.4%)	7 (44%)	8 (50%)	1 (6%)	*0.95*
>5 28 (63.6%)	11 (39%)	15 (53%)	2 (7%)	
Surgical Time Score (CholeS Study Group), *n* (%)				
Low score, 9 (20.4%)	6 (67%)	3 (33%)	0 (0%)	*0.21*
Intermediate score, 32 (72.7%)	12 (37.5%)	17 (53%)	3 (9.4%)	
High score, 3 (6.8%)	0 (0%)	3 (100%)	0 (0%)	
Nassar Score 2019, *n* (%)				
Low score, 11 (25%)	7 (63.6%)	4 (36.4%)	0 (0%)	*0.13*
Intermediate score, 13 (29.5%)	2 (15.4%)	9 (69.2%)	2 (15.4%)	
High score, 20 (45.5%)	9 (45%)	10 (50%)	1 (5%)	

McNemar test was used for qualitative variables. *p*-value<0.05 is considered statistically significant

The mean, median, mode and standard deviation of CLOC score were 7.4, 7, 7 and +/−2.7; respectively. G10 score's mean, median, mode and standard deviation were 2.6, 2, 1 and +/−1.6; respectively. The mean, median, mode and standard deviation of CAAD score were 6.4, 6, 6, +/−2.8, respectively. Mean, median, mode and standard deviation of Nassar score (2019) were 4.3, 4, 3 and +/−2.4; respectively. Finally, Surgical Time Score's mean, median, mode and standard deviation were 4.5, 4.25, 3.5 and +/−1.8; respectively.

Table 5 shows the relationship between the ability of ICG NIRF-C to delineate bile duct anatomy before and after dissecting Calot's triangle and the mentioned scores.

We observed statistically significant differences in the visualization of the CBD using ICG NIRF-C before dissecting Calot's triangle in patients with G10≥3 ($p=0.002$), G10≥5 ($p=0.043$) and Nassar score 2019. Thus, ICG NIRF-C could detect the CBD in 12 patients (48%) with a G10<3 before dissection of Calot's triangle and in only 1 patient (5.3%) with a G10≥3. Similary, ICG NIRF-C could detect the CBD in 13 patients (36%) with a G10<5 before dissection of Calot's triangle and in none of the patients with a G10≥5. Regarding Nassar score 2019, ICG NIRF-C could detect the CBD before dissection of Calot's triangle in 7 patients with low score (63.6%), 1 patient with

Table 5 Relationship between the ability of fluorescence cholangiography to delineate the bile duct anatomy before and after dissection of calot's triangle and CLOC, G10, CAAD risk scores and surgical time score (CholeS study Group) $n = 44$

Before dissection of Calot's triangle							After dissection of Calot's triangle					
	CD, n (%)	*p*	**CBD, n (%)**	*p*	**CDBDJ, n (%)**	*p*	**CD, n (%)**	*p*	**CBD, n (%)**	*p*	**CDBDJ, n (%)**	*p*
CLOC, *n* (%)												
≦6, 17 (38.6%)	0 (0%)	-	6 (35%)	*0.5*	0 (0%)	-	11 (65%)	*0.5*	17 (100%)	-	15 (88%)	*0.5*
>6, 27 (61.4%)	0 (0%)		7 (26%)		0 (0%)		20 (74%)		27 (100%)		22 (81.5%)	
G10, n (%)												
<3, 25 (56.8%)	0 (0%)	-	12 (48%)	*0.002*	0 (0%)	-	18 (72%)	*0.8*	25 (100%)	-	23 (92%)	*0.1*
≥3, 19 (43.2%)	0 (0%)		1 (5.3%)		0 (0%)		13 (68%)		19 (100%)		14 (74%)	
<5, 36 (81.8%)	0 (0%)	-	13 (36%)	*0.043*	0 (0%)	-	25 (69%)	*0.75*	36 (100%)	-	31 (86%)	*0.43*
≥5, 8 (18.2%)	0 (0%)		0 (0%)		0 (0%)		6 (75%)		8 (100%)		6 (75%)	
CAAD, *n* (%)												
≦5, 16 (36.4%)	0 (0%)	-	6 (37.5%)	*0.38*	0 (0%)	-	10 (62.5%)	*0.38*	16 (100%)	-	13 (81%)	*0.7*
>5 28 (63.6%)	0 (0%)		7 (25%)		0 (0%)		21 (75%)		28 (100%)		24 (86%)	
Surgical Time Score (CholeS Study Group), *n* (%)												
Low score, 9 (20.4%)	0 (0%)	-	3 (33%)	*0.5*	0 (0%)	-	7 (78%)	*0.86*	9 (100%)	-	9 (100%)	*0.27*
Intermediate score, 32 (72.7%)	0 (0%)		10 (31%)		0 (0%)		22 (69%)		32 (100%)		26 (81.3%)	
High score, 3 (6.8%)	0 (0%)		0 (0%)		0 (0%)		2 (67%)		3 (100%)		2 (67%)	
Nassar Score 2019, *n* (%)												
Low score, 11 (25%)	0 (0%)	-	7 (63.6%)	*0.009*	0 (0%)	-	7 (63.6%)	*0.41*	11 (100%)	-	11 (100%)	*0.19*
Intermediate score, 13 (29.5%)	0 (0%)		1 (7.7%)		0 (0%)		11 (84.6%)		13 (100%)		11 (84.6%)	
High score, 20 (45.5%)	0 (0%)		5 (25%)		0 (0%)		13 (65%)		20 (100%)		15 (75%)	

McNemar test was used for qualitative variables. p-value < 0.05 is considered statistically significant intermediate score (7.7%) and 5 patients with high score (25%) ($p=0.009$). There were no differences with respect to G10 and Nassar 2019 scores in the visualization of the rest of the biliary structures when using ICG NIRF-C before and after dissection of Calot's triangle.

Regarding CLOC, CAAD scores and Surgical Time Score (CholeS Study Group), there were no differences in the visualization of the the biliary anatomy when using ICG NIRF-C before and after dissection of Calot's triangle (Table 5).

Discussion

ICG ability to highlight blood perfusion and biliary anatomy has proven valuable in numerous surgical procedures, especially during complex cholecystectomies[10–28]. By enhancing the perception of biliary anatomical details, ICG significantly contributes to the precision of LC, thereby reducing the risk of conversion to open surgery, minimizing intraoperative complications such as BDIs, and improving the safety and effectiveness of ambulatory LC [19–23, 26, 28, 31, 32, 34].

This prospective descriptive study evaluated the use of indocyanine green fluorescence cholangiography (ICG-FC) during laparoscopic cholecystectomy (LC) in a cohort of 44 patients stratified by five validated risk scores (CLOC, G10, Nassar-2019, CAAD, and Surgical Time Score). Our primary aim was to determine the ability of ICG-FC to enhance visualization of biliary structures across different levels of operative difficulty.

Impact of ICG on biliary anatomy visualization

In our study, the use of indocyanine green (ICG) near-infrared fluorescence cholangiography (NIRF-C) significantly improved the visualization of key biliary structures, such as the common bile duct (CBD), cystic duct (CD), and cystic duct-bile duct junction (CDBDJ). These structures are essential landmarks in laparoscopic cholecystectomy because their clear identification is crucial for ensuring the critical view of safety, reducing the risk of bile duct injury, and completing the procedure without complications. Pre-dissection, the CBD was visualized in only 29% of cases, but this rate increased to 100% after the dissection of Calot's triangle. This improvement in visualization has significant clinical implications, as it reduces the likelihood of bile duct injuries (BDIs), which are among the most severe complications during laparoscopic cholecystectomy. Similarly, the CD and CDBDJ were identified in 71% and 84% of patients, respectively, after dissection ($p<0.001$ for all comparisons between pre- and post-dissection). These findings were observed in our study, aligning with those of Schols et al. [11], who demonstrated that early biliary tract delineation with ICG facilitates safe surgery, especially in challenging cases (Table 2).

In our study, ICG NIRF-C proved crucial for enhanced visualization of biliary structures, particularly in high-risk patients. Importantly, this enhanced visualization was achieved in a cohort that, although not dominated by acute cholecystitis, included substantial operative complexity. Specifically, patients with **CLOC > 6**, who face increased surgical complexity and a higher likelihood of needing conversion to open surgery, demonstrated notable benefits. These patients, constituting 61.4% of our cohort, exhibited improved delineation of biliary anatomy, which is often challenging to discern in complex cases. Post-dissection visualization rates for these patients were 74% for the cystic duct (CD) and 81.5% for the common bile duct junction (CDBDJ), compared to 65% and 88%, respectively, in patients with CLOC scores of 6 or less. This suggests a differential impact of fluorescence cholangiography based on surgical complexity, although the common bile duct (CBD) was visualized with 100% effectiveness in both groups, highlighting the method's overall reliability. The application of ICG provided real-time fluorescence guidance, significantly reducing the risk of structural misidentification and subsequent surgical complications.

According to our findings, patients with **G10 scores ≥ 3**, which predicts greater difficulty in identifying the biliary anatomy, pre-dissection visualization of the CBD was only 5.3%, compared to 48% in patients with G10 scores < 3. However, after dissection and the use of ICG, the CBD was identified in 100% of all cases, regardless of G10 score ($p=0.002$ for G10 ≥ 3 vs. G10 < 3). This shows that ICG compensates for the difficulties predicted by the G10 score, facilitating clearer visualization in even the most challenging cases. This mirrors the results of Ishizawa et al. [10], who demonstrated that the use of ICG can highlight biliary structures even in difficult cases, reducing the likelihood of BDI [10] (Table 3).

Similarly, in our study, patients with **Nassar scores ≥ 3** had more difficulty visualizing the biliary anatomy before dissection, with only 39% of patients with Nassar scores < 3 having their CBD visualized pre-dissection. After dissection and the use of ICG, the CBD was identified in all patients, regardless of the Nassar score (Table 3), reinforcing the crucial role of ICG in aiding complex surgeries.

Reduction in conversion to open surgery

Although the study was not designed to evaluate conversions or bile duct injury, we observed that all procedures were completed laparoscopically without complications or conversion. This should be interpreted as a secondary, hypothesis-generating finding, consistent with the biological plausibility that improved anatomical visualization (supported by the 100% CBD visualization observed in this study) may help avoid conversion in complex cases. In line with this, one of the most striking observations was the absence of conversions to open surgery in high-risk cases. As mentioned, while our study was not powered to statistically prove a reduction in conversions, this finding is noteworthy when compared to expected conversion rates from external validation studies. Moreover, benchmarking against validated risk scores and historical series is an accepted approach in pilot surgical studies.

According to CLOC score, the risk of conversion to open for low (CLOC ≤ 6) and high risk (CLOC > 6) patients is 1.2% and 7.1%, respectively. Hence, patients identified as high risk have a near six-fold higher rate of conversion than low risk patients [26]. It is notable that in the CLOC study, of the converted patients without intraoperative complications ($N = 214$), conversion was due to procedural difficulty (Nassar grade 3–4 or bile duct exploration) in the majority of cases (96%) [26]. Consequently, in patients with significant inflammation and/or fibrosis in the region of Calot's triangle, accurate identification of anatomical landmarks may prove difficult or impossible using a laparoscopic approach [26].

In line with it, of the 27 patients (61,4%) with CLOC score > 6 in our serie, at least 2 patients should had been converted to open surgery. No conversions to open surgery were observed in these high-risk cases, underscoring the effectiveness of ICG in this context.

Similarly, the **G10 score** showed that 43.2% of patients in this study had scores ≥ 3, which typically correlates with more challenging procedures. Despite this, ICG allowed for safe completion of all procedures laparoscopically without conversion to open surgery. Patients with **G10 scores ≥ 5** have a 33% expected conversion rate [27]. Thus, of our 8 patients (18,2%) with G10 score ≥ 5, at least 2 of them should had been converted to open surgery. Nevertheless, they did not experience any conversions in this study, further demonstrating the effectiveness of ICG in managing complex cases.

The probability of observing zero conversions in these subgroups, though not impossible, is relatively low (approximately 13.7% for CLOC > 6, and 4.1% for G10 ≥ 5). We therefore interpret these findings as hypothesis-generating: they support the biological plausibility that improved visualization of critical structures may help avoid conversion, but definitive demonstration would require larger randomized trials.

For predicting LC difficulty, Nassar Score (2019) offers the best balance of predictive accuracy, validation, and practical utility. Given its broad applicability and rigorous validation, this model may serve as the most reliable tool for preoperative risk assessment in patients undergoing LC [30]. According to this, intermediate scores (3–4 points) up to 40% likelihood of some difficulties, suggesting a moderate risk of conversion; and high scores (≥ 5 points) have over 80% chance of difficulties, often necessitating conversion to open surgery [30]. In our serie 13 patients (29,5%) had a intermediate score and 45.5% of patients had a high score. Despite this, ICG facilitated completion of all procedures laparoscopically, with no conversions observed. While this finding is notable, it should be interpreted as hypothesis-generating rather than confirmatory. This echoes the conclusions of Nassar et al. [30], who emphasized the importance of using advanced visualization techniques, such as ICG, to manage the challenges associated with high-risk patients (Table 2). This result is also strongly supported by the findings of Sutcliffe et al. [27], who noted that improved visualization of biliary structures with fluorescence-guided surgery can significantly reduce conversion rates. In patients with **Nassar scores ≥ 5**, who represent the most complex and difficult cases, the absence of conversions is particularly noteworthy. Studies by El-Sharkawy et al. [23] and Osayi et al. [23] corroborate this finding, demonstrating that ICG significantly reduces the risk of conversion in high-complexity cases by providing better visualization of the bile ducts and surrounding tissues, allowing surgeons to navigate through adhesions and anatomical challenges without resorting to open surgery.

Reduction in operative time

In our study, we hypothesized that the use of indocyanine green may improve surgical times even in intermediate/high risk cases by allowing better visualization of biliary structures and increasing the surgeon's confidence. In this manner, one of the most compelling findings of our study is the reduction in operative time when ICG is used. As detailed in Table 4, ICG NIRF-C also contributed to a significant reduction in operative time, especially in high-risk patients. On average, surgeries in this study lasted 45 ± 15 minutes, with 56% of patients with **G10 scores < 3** completing surgery in less than 45 min. However, the impact of ICG is even more pronounced in patients with **G10 scores ≥ 3**, where only 16% of patients had surgeries exceeding 90 min ($p = 0.01$). This reduction in operative time has important implications for postoperative outcomes, including a potentially lower risk of complications and improved efficiency in the use of operating room resources, which are critical factors in optimizing surgical workflows. This is in line with Tsutsui et al. [15], who found that the use of ICG reduced surgery times by improving intraoperative decision-making and dissection efficiency.

Patients with **G10 scores ≥ 5**, who typically face a 33% conversion rate and longer surgery durations [27], saw operative times reduced significantly with ICG. Only 7% of these high-risk patients required more than 90 min for surgery ($p = 0.03$). These results align with and expand upon the findings from the CholeS Study Group [29], which demonstrated that preoperative factors could predict longer surgeries. Our study builds on this by showing how the use of ICG mitigates these risks specifically through enhanced intraoperative visualization, resulting in improved outcomes even in high-complexity cases (Table 4).

The impact of ICG in reducing operative time was also evident in patients classified with higher **Surgical Time Score**, a score validated in an independent cohort of 2405 patients and demonstrating good predictive capacity, with an area under the ROC curve of 0.708 [29]. According to the CholeS Study Group, surgeries in patients with intermediate or high-risk scores are expected to exceed 90 min, but in this study and contrary to what might be expected, none of the high-risk patients had surgeries lasting over 90 min, thanks to the use of ICG. Bharamgoudar et al. [29] highlighted similar outcomes, where ICG helped reduce surgical times and improve resource allocation in complex cholecystectomy cases. Additionally, Sugrue et al. [26] demonstrated that accurate intraoperative visualization, especially in cases deemed complex by scores such as G10 and the Surgical Time Score (CholeS Study Group), can significantly reduce operative times, which directly correlates with our findings (Table 5).

Expected percentage of candidate interventions for outpatient surgery according to CAAD score

A CAAD score of ≦5 is associated with 80.8% successful day-case cholecystectomy compared with 19.2% associated with a CAAD score > 5 ($p < 0.001$) [28]. In terms of ambulatory surgery eligibility, 63.6% of our patients had **CAAD scores > 5**, a group that typically has only a 19.2% chance of successful day-case surgery. Despite this, ICG allowed for the safe discharge of all patients the day after surgery, suggesting that ICG can help expand the eligibility for ambulatory cholecystectomy. In our serie, there were no day-case surgeries but in all patients LC was performed safely with the visualization of CBD in all surgeries and all patients were discharged the next day after surgery without postoperative complications or readmissions. This finding is supported by El-Sharkawy et al. [28], who demonstrated that the use of ICG in high-risk day-case surgeries can significantly improve outcomes by reducing the incidence of complications that typically necessitate prolonged hospital stays (Table 5).

As a final remark, it is important to consider the role of ICG NIRF-C in relation to intraoperative cholangiography (IOC). Although comparative studies showed equivalent biliary visualization and complications comparing ICG NIRF-C with intraoperative cholangiography, with even higher CBD visualization using ICG [33], we do not regard fluorescence as a replacement for IOC; rather, both should be considered complementary. IOC remains valuable for ductal mapping, lithiasis detection and for confirming suspected bile duct injury, especially in high-risk or complex cases. On the other hand, ICG NIRF-C provides continuous, real-time imaging without radiation or cystic duct cannulation, which may be particularly advantageous in difficult or inflamed cases where cannulation is not feasible. Besides, from a practical standpoint, barriers are minimal: ICG is inexpensive, requires no additional training (simply a bolus after induction), and most modern laparoscopic towers already incorporate fluorescence capability. Future comparative studies are needed to define the optimal integration of these techniques in routine practice.

Conclusion

In this prospective descriptive study, a very low dose of indocyanine green enabled excellent biliary visualization during LC, which was the primary endpoint. The CBD was identified in 100% of patients after dissection, and both the cystic duct and the CD–CBD junction were visualized in the majority. Secondary observations included the absence of complications, conversions and a favorable operative-time profile, even in patients with high predicted surgical difficulty according to multiple validated scoring systems. These findings support the integration ICG- NIRF-C as a valuable tool to enhance biliary visualization, particularly in complex cases, while larger randomized trials are needed to determine its definitive impact on conversions and bile duct injury.

Limitations of the study

This study has several limitations. Firstly, it was a prospective, single-arm descriptive study without a randomized control group, which would have provided greater validity to our conclusions. Secondly, the sample size was modest, as it was powered specifically for biliary visualization rather than for rare outcomes such as bile duct injury or conversion. To demonstrate additional objectives, such as a potential reduction in BDIs, a larger sample would be required. Moreover, external validation of the use of ICG in high-risk scores would be valuable to corroborate the hypothesized associations. Generalizability to urgent or emergent cholecystectomy is also limited and should be assessed in future prospective studies. Finally, as a topic for further research, it would be of interest to develop a new risk score for conversion to open surgery that incorporates the biliary anatomy identified with ICG NIRF-C.

Author contributions Natalia Pujol-Cano, Elías Palma-Zamora, Jaume Bonnin-Pascual, and Magdalena Coll-Sastre contributed to data acquisition. Natalia Pujol-Cano and Francesc Xavier Molina-Romero conceived the study idea, drafted the manuscript, and performed the statistical analysis. José Miguel Morón-Canis, Francesc Xavier González-Argenté, and Francesc Xavier Molina-Romero supervised the study and performed the final revision of the manuscript. All authors reviewed and approved the final version of the manuscript.

Data availability No datasets were generated or analysed during the current study.

Declarations

Competing interests The authors declare no competing interests.

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