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Original Research Article

Optimal timing for preoperative indocyanine green administration to enhance fluorescent cholangiography during laparoscopic cholecystectomy: a prospective study

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ABSTRACT

Background: Safe and accurate visualization of biliary anatomy is essential during laparoscopic cholecystectomy. Indocyanine green (ICG) fluorescence cholangiography has emerged as a valuable tool to delineate critical structures and reduce the risk of bile duct injury. While earlier studies recommended ICG administration 8–24 hours prior to surgery, recent evidence suggests that shorter intervals may be equally effective. This prospective study compared the efficacy of ICG fluorescence cholangiography administered 4 hours versus 8 hours before laparoscopic cholecystectomy, focusing on the clarity of biliary visualization, operative outcomes and patient recovery.
Methods: Sixty patients undergoing elective laparoscopic cholecystectomy were randomized into two groups: Group A (ICG administered 4 hours preoperatively) and Group B (8 hours). A standardized scoring system assessed visualization of the cystic duct and common bile duct. Operative duration, complications and recovery were secondary outcomes.
Results: Both groups showed high rates of optimal biliary tract visualization (≥4/5 score): 90% in Group A and 93.3% in Group B (p=0.64). Mean operative times were similar (48.3±8.5 vs. 46.9±7.9 minutes; p=0.42). No major bile duct injuries occurred. Postoperative complication rates and hospital stays were also comparable.
Conclusions: ICG administration as early as 4 hours before surgery provides biliary visualization equivalent to the conventional 8-hour interval. This shorter window may enhance scheduling flexibility without compromising safety or image quality. Further multicentre studies are recommended to validate these findings.

Keywords: Biliary imaging, Fluorescent cholangiography, Indocyanine green, Laparoscopic cholecystectomy, ICG timing

INTRODUCTION

Laparoscopic cholecystectomy is the standard procedure for managing symptomatic gallstone disease, largely due to its minimally invasive nature and favourable patient outcomes.[1]

Despite its routine use, the risk of accidental bile duct injury remains a serious concern, potentially leading to extended hospitalization, long-term complications and higher healthcare costs.[2] Surgeons thus rely on clear visualization of biliary anatomy to minimize these risks. Indocyanine green (ICG) is a fluorescent dye that becomes visible under near-infrared (NIR) light once it is excreted into bile.[3] By capitalizing on specialized laparoscopic imaging systems, surgeons can identify key structures such as the cystic duct, common hepatic duct and common bile duct (CBD) in real time.[4] Compared to traditional intraoperative cholangiography, which involves radiation and direct cannulation of the cystic duct, ICG fluorescence cholangiography provides a radiation-free and potentially simpler alternative.[5] One crucial factor in harnessing the full potential of ICG fluorescence is the timing of its administration. Historically, studies have advocated for injection 8–24 hours before surgery to ensure robust fluorescence within the biliary tree.[5]

However, this extended window can be inconvenient for patients and clinical teams, especially when schedules shift or semi-urgent procedures arise.[6] Preliminary evidence indicates that shorter intervals, such as 4 hours, might suffice without compromising image quality.[7] If validated, this more flexible approach could streamline patient preparation and operating room logistics.

Rationale for indocyanine green use

ICG fluorescence cholangiography allows for dynamic, real-time mapping of the biliary tree, helping surgeons distinguish vital structures and minimize the risk of misidentification.[8] Because ICG is exclusively metabolized by the liver and excreted in bile, it highlights the biliary channels under near-infrared imaging.[9] Surgeons can thus visualize these pathways with high contrast, often obviating the need for traditional radiographic cholangiography and reducing overall operative complexity.

Study objective

The primary objective of this prospective study was to determine whether a 4 hours interval between ICG administration and laparoscopic cholecystectomy is non-inferior to the conventional 8 hours interval in terms of the quality of biliary fluorescence. Secondary objectives included examining operative times, rates of conversion to open surgery, intraoperative complications and postoperative outcomes.

Hypothesis

Authors hypothesized that patients receiving ICG 4 hours before surgery would exhibit biliary fluorescence comparable to that of patients receiving ICG 8 hours preoperatively, thereby offering a viable alternative that might simplify scheduling and reduce patient inconvenience.

METHODS

Study design and ethical approval

This single-centre, prospective trial was conducted at Indraprastha Apollo Hospitals, New Delhi, a high-volume surgical unit specializing in laparoscopic gastrointestinal procedures. The study was carried out over a 14-month period, from September 2022 to October 2023.

The protocol received approval from the Institutional Review Board and all participants provided written informed consent, in accordance with the principles outlined in the Declaration of Helsinki.[10]

Patient enrolment

Individuals aged 18–75 years with symptomatic gallstones or biliary colic were evaluated for inclusion. Exclusion criteria comprised severe hepatic dysfunction (Child-Pugh B or C), hypersensitivity to ICG or iodine, pregnancy or lactation, prior biliary surgery and urgent or emergent cholecystectomies for acute cholecystitis or cholangitis. A total of 60 eligible patients were recruited over a specified timeframe.

Randomization and intervention

Participants were assigned via computer-generated randomization into two groups.

Group A

ICG administered 4 hours before surgery (n=30).

Group B

ICG administered 8 hours before surgery (n=30).

Each patient received 0.25 mg/kg of ICG, diluted in 10 ml of normal saline and given intravenously over 2–3 minutes. Preoperative fasting of at least 6 hours was maintained per standard hospital protocols.

Surgical technique

All laparoscopic cholecystectomies were performed under general anaesthesia by senior surgeons experienced in advanced minimally invasive procedures. Pneumoperitoneum was established using either a Veress needle or open technique at the umbilicus, followed by the placement of four standard trocars. NIR imaging capabilities were employed to detect ICG fluorescence in the biliary tree.

The surgical procedure began with a white-light laparoscopic survey of the gallbladder and surrounding anatomy. The laparoscope was then switched to near-infrared mode to visualize the cystic duct, CHD and CBD and the fluorescence intensity and clarity were documented. Dissection of Calot's triangle proceeded until the critical view of safety was achieved. Once the cystic duct and artery were clearly identified, they were clipped and divided. The gallbladder was separated from the liver bed and extracted. A final assessment ensured hemostasis and biliary integrity before concluding the procedure.

Outcome measures

The primary outcome of this study was the quality of fluorescence visualization, assessed using a five-point scale denoting no fluorescence, for weak fluorescence with difficult identification of structures, for moderate fluorescence with some difficulty in identification, for strong fluorescence with easy identification and for very strong fluorescence with distinctly outlined structures. A score of 4 or more for each major biliary component was considered optimal visualization. Secondary outcomes included operative time (defined from skin incision to skin closure), conversion to open surgery, intraoperative complications such as bile duct injury, bleeding or gallbladder perforation and postoperative complications occurring within 30 days, including infections, bile leaks or readmissions. Hospital stay was measured from the day of surgery to discharge.

Statistical methods

Data analysis was carried out using SPSS (version XX, IBM Corp., Armonk, NY). Continuous variables were expressed as mean±standard deviation (SD) and assessed using Student's t-test. Categorical data were represented as counts (percentages) and analysed with chi-square or Fisher's exact tests, where appropriate. Statistical significance was set at $p<0.05$. The sample size of 60 (30 per group) was chosen based on an anticipated 20% difference in visualization quality, aiming for 80% power at a 0.05 alpha level.

RESULTS

Patient demographics

Sixty patients (30 in each group) completed the study without loss to follow-up. (Table 1) outlines the baseline demographic and clinical characteristics, which were comparable between Group A and Group B.

Biliary visualization scores

No statistically significant difference was noted in the primary endpoint biliary visualization scores. In Group A, 27 of 30 patients (90%) achieved an optimal fluorescence score (≥4) for all major biliary structures, while in group B, 28 of 30 patients (93.3%) met the same criterion ($p=0.64$). Mean scores for the cystic duct, CHD and CBD were also similar (Table 2). The proportion of patients achieving optimal visualization (score≥4) for each major biliary structure is illustrated in (Figure 1). Stacked bar chart depicting the number of patients in each group (A and B) who achieved optimal (score≥4) versus suboptimal (score<4) fluorescence visualization for three key biliary structures: cystic duct, common hepatic duct (CHD) and common bile duct (CBD).

Group A (ICG administered 4 hours preoperatively) and Group B (ICG administered 8 hours preoperatively) each comprised 0 patients. Blue and red bars indicate optimal visualization scores in Group A and Group B, respectively, while the lighter shades represent suboptimal outcomes. The visualization success was high across both groups, supporting non-inferiority of the 4 hours protocol. Figure 1 visually reinforces the primary study outcome: comparable efficacy of shorter and conventional ICG timing protocols in delineating biliary anatomy during laparoscopic cholecystectomy.

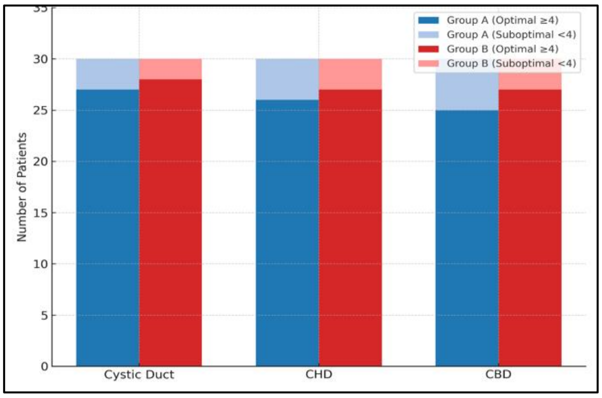

Figure 1: Optimal vs suboptimal visualization by biliary structure.

Operative time and conversion

Operative durations were comparable between the two cohorts.

Group A: 48.3±8.5 minutes, Group B: 46.9±7.9 minutes ($p=0.42$).

No patient in either group required conversion to open surgery, reflecting both the technical proficiency of the surgical team and the utility of near-infrared fluorescence guidance.

Intraoperative complications

There were no instances of major bile duct injuries in this series. Group A had one patient with minor bleeding from the gallbladder bed, which was controlled laparoscopically. Group B had a single case of gallbladder perforation leading to spillage of bile the area was thoroughly irrigated and no subsequent infection developed. Neither event was attributed to inadequate visualization of the biliary tree.

Postoperative outcomes

Complications following surgery were minimal and evenly distributed between groups. One patient in each group developed a superficial wound infection, resolved with oral antibiotics. No bile leaks or major infections were documented. The average hospital stay was similarly brief group A: 1.8±0.6 days, group B: 1.7±0.5 days ($p=0.53$). All patients resumed oral intake the day after surgery and were discharged once they demonstrated stable vital signs and tolerated a regular diet. A comprehensive summary of operative and postoperative outcomes is provided in Table 3.

Table 1: Baseline demographic and clinical characteristics of patients in Group A (ICG 4 hours preoperative) and Group B (ICG 8 hours preoperative).

Variable	Group A (n=30)	Group B (n=30)	P value
Age (years, mean±SD)	45.2±12.3	44.7±11.8	0.85
Gender (M/F)	12 / 18	10 / 20	0.59
BMI (kg/m²)	26.5±3.2	26.7±3.1	0.76
ASA Score (I/II/III)	18 / 10 / 2	17 / 11 / 2	0.91
Liver function tests	Normal in all	Normal in all	-

Table 2: Comparison of biliary fluorescence visualization scores for major biliary structures (cystic duct, common hepatic duct, common bile duct) between groups.

Biliary structure	Group A	Group B	P value
Cystic duct	4.2±0.6	4.3±0.5	0.67
Common hepatic duct	4.1±0.7	4.2±0.6	0.72
Common bile duct	4.0±0.7	4.1±0.8	0.74
Patients with score ≥4	27/30 (90.0%)	28/30 (93.3%)	0.64

Table 3: Operative and postoperative outcomes (operative time, conversion rate, complications, hospital stay) for both groups.

Outcome	Group A	Group B	P value
Operative time (min, mean±SD)	48.3±8.5	46.9±7.9	0.42
Conversion to open surgery	0	0	-
Intraoperative complications	1 (minor bleeding)	1 (gallbladder perforation)	-
Postoperative wound infections	1	1	-
Bile duct injury	0	0	-
Length of hospital stay (Days±SD)	1.8±0.6	1.7±0.5	0.53

Subgroup insights

Subgroup evaluations, such as for patients with a BMI ≥30 kg/m^2 or those showing mild hepatic steatosis on imaging, did not reveal any significant deviations in fluorescence scores or operative times. These observations suggest that a 4 hours ICG protocol remains effective across varied patient profiles.

DISCUSSION

ICG fluorescent cholangiography has increasingly become a valuable tool for laparoscopic cholecystectomy, offering a clear, real-time view of the biliary network without relying on ionizing radiation.[12] By helping surgeons identify and protect vital structures, it potentially reduces operative risk and improves overall efficiency. This study sought to explore whether administering ICG 4 hours preoperatively could match the standard 8 hours interval in terms of visualization quality.

Main findings

Our data show that a 4 hours ICG interval provided biliary fluorescence on par with the conventional 8-hour timeframe. Over 90% of patients in both groups met the threshold for optimal visualization. These results imply that a more condensed preoperative schedule does not compromise the ability to delineate biliary structures.

Impact on clinical practice

The option to administer ICG closer to surgery offers logistical advantages, particularly for hospitals with high patient volumes or unpredictable operating room schedules.[13] Should an operating schedule change or an earlier surgical slot become available, a shorter interval ensures that ICG administration can still take place without significant loss of fluorescence quality.

Pharmacokinetic considerations

ICG is rapidly cleared from the bloodstream by hepatocytes and secreted into bile, often achieving strong fluorescence within hours.[14] Our findings support that by 4 hours, enough dye is present in the biliary system to yield robust imaging. This contrasts with older recommendations that favored an 8–24 hours lead time suggesting that earlier protocols may have been overly conservative.[5,9]

Comparison to prior research

Previous investigations generally supported administering ICG many hours before surgery to maximize fluorescence.[5,9] However, smaller-scale studies hinted that a shorter interval might be sufficient.[15] Our prospective trial, which enrolled a larger cohort, offers more compelling evidence that a 4 hours schedule can achieve similar outcomes.

Limitations

While the results are promising, several limitations warrant mention.

Single-centre scope

Conducting the study at one institution may limit the generalizability of the findings.

Exclusion of complex cases

Patients with acute cholecystitis, cholangitis or advanced liver disease were not included.

Relatively modest sample size

Although 60 patients per group met the power calculation for our primary endpoint, larger, multicentre studies would further validate these conclusions.

Economic considerations

We did not conduct a formal cost-effectiveness analysis, which might be relevant for broader adoption.

Future directions

Multicentre collaboration

Larger-scale trials in diverse populations could strengthen the evidence for using a 4-hour protocol.

Complex biliary conditions

Research is needed to determine if similar results can be replicated in patients with acute inflammation or altered anatomy.

Cost analysis

Evaluating the financial implications of different ICG protocols could guide widespread implementation.

Dose refinement

Additional studies might investigate lower or higher doses of ICG, especially in patients with unique metabolic profiles.

CONCLUSION

This prospective trial indicates that administering ICG 4 hours before laparoscopic cholecystectomy can deliver biliary fluorescence equivalent to the more traditional 8 hours interval. Surgeons and patients may benefit from the added scheduling flexibility, reduced waiting times and maintained surgical safety. While further research, particularly in multicentre settings, is needed to corroborate these findings, the present data strongly suggest that a 4 hours protocol is both feasible and effective.

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Ethical approval: The study was approved by the Institutional Ethics Committee

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