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Application of Indocyanine Green Fluorescence Imaging During Laparoscopic Reoperations of the Biliary Tract Enhances Surgical Precision and Efficiency

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Background: A history of abdominal surgery is considered a contraindication for laparoscopic procedures. However, the advancements in laparoscopic instruments and techniques have facilitated the performance of increasingly intricate operations, even in patients with prior abdominal surgeries. ICG fluorescence imaging technology offers advantages in terms of convenient operation and clearer intraoperative bile duct imaging, as confirmed by numerous international clinical studies on its feasibility and safety. The application of ICG fluorescence imaging technology in repeat laparoscopic biliary surgery, however, lacks sufficient reports.

Methods: The clinical data of patients who underwent elective reoperation of the biliary tract in our department between January 2020 and June 2022 were retrospectively analyzed. ICG was injected peripherally before the operation, and near-infrared light was used for 3-dimensional imaging of the bile duct during the operation.

Results: Altogether, 143 patients were included in this study and divided into the fluorescence and nonfluorescence groups according to the inclusion criteria. Among the 26 patients in the fluorescence group, cholangiography was successfully performed in 24 cases, and the success rate of intraoperative biliary ICG fluorescence imaging was 92.31%. The intraoperative biliary tract identification time was significantly different between the fluorescence and nonfluorescence groups, but no statistical difference was observed in the final operation method, operative time, and intraoperative blood loss between the 2 groups. Although there was no significant difference in the postoperative ventilation rate, incidence of bile leakage, and stone recurrence rate at 6 months postoperatively between the 2 groups ($P > 0.05$), a significant difference in postoperative hospitalization days was observed ($P = 0.032$).

Conclusion: The application of ICG fluorescence imaging technology in laparoscopic reoperation of the biliary tract is useful for the early identification of the biliary tract during operation, thereby shortening the operative time and reducing the risk of damage to nonoperative areas. This approach also enhances the visualization of the biliary system and avoids secondary injury intraoperatively due to poor identification of the biliary system. This technique is safe for repeat biliary tract surgery and has a good application prospect.

Key Words: indocyanine green fluorescence imaging, intraoperative navigation, laparoscopic reoperation of biliary tract

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A history of abdominal surgery is considered a contraindication for laparoscopic procedures.[1–3] However, the advancements in laparoscopic instruments and techniques have facilitated the performance of increasingly intricate operations, even in patients with prior abdominal surgeries.[4–6] The laparoscopic repeat biliary surgery presents 2 challenges, which are as follows: trocar placement becomes difficult due to previous biliary laparotomy, and exposure of the biliary duct after multiple surgeries poses a considerable challenge.[7,8] Indocyanine green (ICG) is a molecular dye that specifically binds to plasma proteins and lipoproteins, exhibiting fluorescence upon irradiation in the near-infrared range (750 to 810 nm).[9] Before surgery, the intravenous administration of ICG is followed by subsequent elimination through the biliary system.[10] Intraoperative real-time visualization of the biliary tract was conducted. Compared with intraoperative cholangiogram (IOC), ICG fluorescence imaging technology offers advantages in terms of convenient operation and clearer intraoperative bile duct imaging, as confirmed by numerous international clinical studies[11–13] on its feasibility and safety. The application of ICG fluorescence imaging technology in repeat laparoscopic biliary surgery, however, lacks sufficient reports.

The primary objective of the study was to investigate the feasibility of employing the ICG technique in repeat laparoscopic biliary surgery with the aim of augmenting the success rate of this surgical procedure.

METHODS

Patients

The present study is a retrospective analysis conducted at a single center. The patients enrolled in this study received medical treatment at our hospital between January 2020 and June 2022. The patient inclusion criteria were as follows: (1)

relevant surgical history involving laparotomy or laparoscopic procedures on the biliary tract; (2) preoperative diagnosis of benign lesions is established by considering the patient's medical history and abdominal imaging findings; (3) the patient is eligible for laparoscopic surgery without any absolute surgical contraindications; (4) the liver function test shows Child-Pugh grade A or B liver disease; (5) comprehensive clinical data are available, encompassing a minimum follow-up period of 6 months; and (6) preoperative imaging data are utilized for the measurement of an extrahepatic bile duct diameter of ≥ 1.0 cm. The exclusion criteria were as follows: (1) people with allergies to ICG preparations or iodine; (2) patients with liver function test results showing Child-Pugh grade C liver disease; (3) patients diagnosed with malignant biliary tract lesions; (4) patients with dysfunction in other organs; (5) those who had undergone combined resection of multiple organs. The ethics committee of our hospital granted approval and authorization for conducting this study (ethics approval number: kyfey20221902). The patients and their families provided written informed consent before study participation.

Preoperative Evaluation

All the patients in both groups underwent blood testing, abdominal ultrasound examinations, magnetic resonance imaging, and magnetic resonance cholangiopancreatography (MRCP). If necessary, an upper abdominal CT scan was performed to assess the condition of the biliary tract.

Administration Modality of ICG

The near-infrared fluorescence imaging system employs the Stryker 1588 AIM camera system (United States), which incorporates the ICG powder (2.5 mL; Rui Du, Dandong, China) for injection.

The ICG fluorescence imaging methods were implemented as follows: (1) before surgery, a skin test was performed to assess for potential allergies; (2) the ICG injection was prepared by combining 25 mg of ICG standby with 10 mL of sterilized water for injection; and (3) the administration procedure involved injecting 2 mL (5 mg) of the ICG solution into the cubital vein 60 minutes before the operation.

Surgical Procedure

After ensuring successful endotracheal intubation and induction of general anesthesia, the patient was placed in a reverse Trendelenburg position. Following the identification of the previous surgical incision, the observation port was meticulously located under direct visualization at a distance of 8 cm from the original incision site. Before commencing laparoscopic surgery, a comprehensive assessment of abdominal adhesions was conducted in a fan-shaped pattern centered around the operative field, following the surgeon's customary practice and preoperative planning (Figs. 1, 2).

Laparoscopic Common Bile Duct Exploration

After exposing the bile duct, a subendoscopic knife was used to make a vertical incision of ~1.0 cm in the common bile duct. Subsequently, a 5.0-mm fiber choledochoscope (Olympus) was inserted through the incision for inspection and extraction of stones within the duct. Following the irrigation of the common bile duct with a normal saline solution, a T-tube was placed at the incision site and interrupted suturing using absorbable 4/0 sutures was performed.

Laparoscopic Choledochojejunostomy

The 5-trocar technique is commonly utilized to expose the biliary duct. In patients who had previously undergone bilioenterostomy, the primary bile duct anastomosis will be exposed. Following the opening of the anastomosis, an intraoperative choledochoscope will be used to extract stones and verify the absence of intrahepatic bile duct stenosis. The bile duct with scar stenosis at the anastomosis will be excised, and the bile duct orifice will be incised and enlarged for anastomosis. The length of the entire afferent loop is measured. If the original length of the afferent loop is < 40 cm, it will be resected again for reconstruction; if the length ranges from 45 to 60 cm, choledochojejunostomy can be performed using absorbable sutures without tension in the afferent loop. The placement of the T-tube and abdominal drainage tube was determined based on the intraoperative circumstances. If the patient has not previously undergone choledochojejunostomy, the bile duct is transected under endoscopy based on literature guidelines.[11] The stones are then removed through the transected bile duct by endoscopy and using biliary lithotomy forceps. A 5.0-mm fiber choledochoscope (Olympus) is utilized in the stone removal procedure; then, the bile duct is rinsed with normal saline. Finally, absorbable 4/0 sutures are used to ensure an anterior wall discontinuity without tension from the input loop. Roux-en-Y anastomosis was performed on the posterior wall, and the placement of the T-tube and abdominal drainage tube was determined based on intraoperative conditions. All surgeons involved in this study were medical team leaders with the capability to independently perform laparoscopic liver, biliary tract, and pancreatic surgeries. They had successfully completed over 20 similar procedures autonomously.

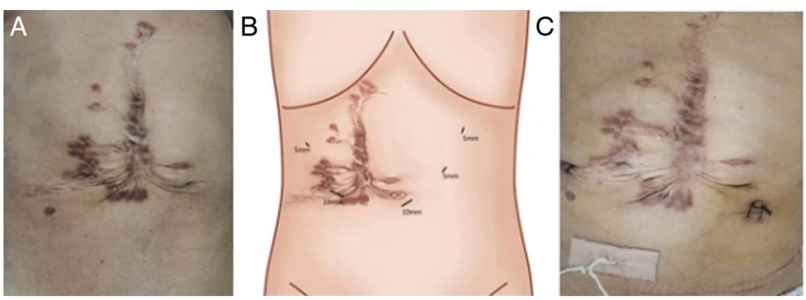

FIGURE 1. A, Preoperative scar on the abdomen. B, The diagram of the Trocar. C, The postoperative condition of the abdomen.

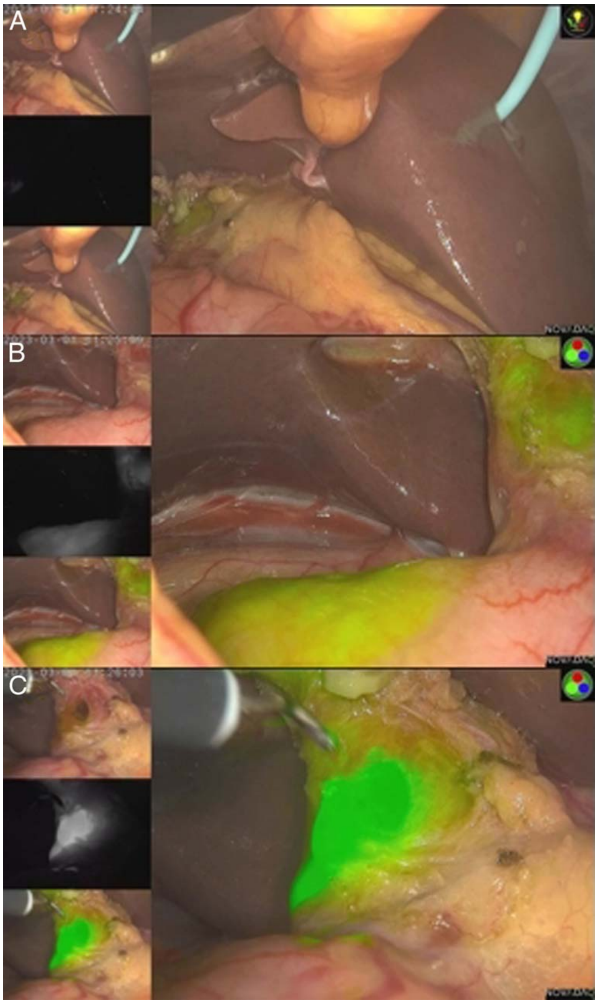

FIGURE 2. A, The ICG was administered through percutaneous transhepatic cholangiography (PTCD). B, The fluorescence was observed in the common bile duct and a section of the duodenum. C, When the common bile duct was dissected, the bile showed strong fluorescence.

Observation Index and Standard

The success rate of biliary tract imaging achieved using the ICG fluorescence imaging system, surgical technique used, surgical duration, intraoperative blood loss, incidence of intraoperative complications, length of hospital stay, and occurrence of postoperative complications were investigated. Outpatient and telephone follow-ups were conducted to assess the long-term complications and quality of life of patients postoperatively. The postoperative follow-up of 6 months was completed in all patients, with the longest recorded follow-up period being 17 months.

Definition

The operative duration was documented based on the anesthesia record sheet, encompassing the entire process from skin incision to closure of all incisions. The estimation of intraoperative blood loss is based on the singular recorded amount of blood loss in the anesthesia record. The bile duct identification time is defined as the duration from the insertion of laparoscopic or laparotomy openings until the successful bile duct opening. Postoperative bile leakage was defined according to the International Liver Surgery Study Group grading standards.[14] Delayed gastric emptying was defined according to the standard definition developed by the International Pancreatic Surgery Research Group in 2007.[15] Postoperative residual stones were defined as bile duct stones identified within 6 months of initial treatment. The bile duct stones detected at >6 months after the first treatment were defined as recurrent stones.[16] Postoperative complications were identified according to the Dindo-Clavien classification standard of surgical complications,[17] with minor complications classified as Clavien graded I to II and severe complications classified as Clavien grade III to V.

Data Analysis

Measurement data were expressed as mean ± SD, and group comparison was performed using the Student *t* test or Mann-Whitney *U* test. The count data were expressed as rates, and group comparison was performed using the Pearson χ^2 or the Fisher exact test. $P<0.05$ was considered statistically significant. Statistical analysis was performed using SPSS 26.0.

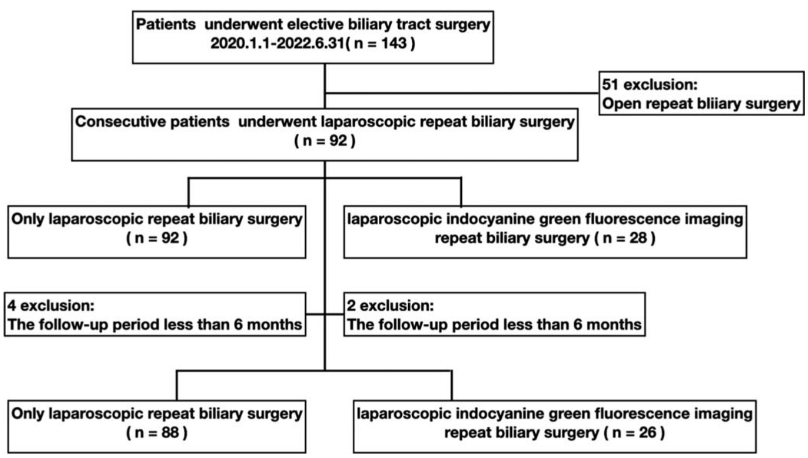

FIGURE 3. Flow chart of study enrollment.

RESULTS

Patient Characteristics

Altogether, 143 patients who underwent elective biliary tract surgery were admitted to our department between January 2020 and June 2022. Among the 92 patients who underwent repeat laparoscopic biliary surgery, 28 patients underwent laparoscopic ICG fluorescence imaging during treatment, whereas 6 patients were excluded due to incomplete postoperative follow-up data. A total of 114 patients were included in the present study (Fig. 3). The demographic characteristics of the 2 patient groups in this study are presented in Table 1. Detailed information regarding previous surgical methods and surgical frequency of the 2 groups are presented in Table 2.

Intraoperative State

Among the 88 patients in the nonfluorescence group of this study, 37 patients underwent LCBDE 32 patients underwent primary-LCDJ, and 19 patients underwent repeat-LCDJ. The average operative time was 153.83 ± 56.97 minutes, the average intraoperative biliary duct identification time was 39 ± 26.42 minutes, and the average intraoperative blood loss was 123.16 ± 97.29 mL. Among them, the biliary duct could not be safely identified under laparoscopy in 1 patient due to severe deformation and adhesion of the hepatic hilar; thus, this case was converted to laparotomy. Of the 26 patients in the fluorescence group, biliary tract imaging was successful in 24 patients (Fig. 3), indicating a success rate of 92.31%. The fluorescence failed to accurately visualize the biliary tract in 2 cases due to the presence of anastomotic stones and a high anastomotic location following previously undergone choledochojejunostomy. Among the 26 patients in the fluorescence group, 16 underwent LCBDE, 6 underwent primary-LCDJ, and 4 underwent repeat-primary-LCDJ. The mean operative and intraoperative biliary tract identification times were 127.64 ± 26.27 and 25 ± 12.27 minutes, respectively. The mean intraoperative blood loss was 90.87 ± 62.95 mL. In the fluorescence group, 1 patient had laparotomy due to severe gastric antrum and hepatic hilar adhesion, which made it impossible to safely dissect the bile duct through a laparoscopic approach. There were no significant differences in the final operation method, operative time, intraoperative blood loss, and conversion rate of laparotomy between the 2 groups, but there were significant differences in the intraoperative biliary duct identification time between the 2 groups (39 ± 26.42 vs. 25 ± 12.27 min; $P = 0.036$), as shown in Table 3.

TABLE 2. Data on Previous Operations and Operative Times of the Fluorescence and Nonfluorescence Groups

Previous surgical data	Nonfluorescent group (N = 88), n (%)	Fluorescent group (N = 26), n (%)	*P*
The previous operation			
LCBDE	66 (76.74)	14 (53.83)	0.792
LCDJ	6 (6.98)	3 (11.54)	0.881
LPD	3 (2.27)	2 (7.69)	0.484
OCBDE	8 (9.09)	4 (15.38)	0.926
OCDJ	3 (3.41)	2 (7.69)	0.741
OPD	2(2.27)	1 (3.85)	0.594
The count of preceding operations			
Once	72 (81.82)	19 (73.08)	0.955
Twice	14 (15.91)	5 (19.23)	0.859
More than twice	2 (2.27)	2 (7.69)	0.468

OCBDE indicates open common bile duct exploration; OCDJ, open choledochojejunostomy; OPD, open pancreaticoduodenectomy.

Postoperative Recovery

In the present study, there were no significant differences between the 2 groups in the incidence of postoperative ventilation, bile leakage, and stone recurrence at 6 months postoperatively ($P > 0.05$). Although there was no significant difference in the Clavein-Dindo grades of the postoperative complications between the 2 groups ($P > 0.05$), 1 patient in the fluorescence group died postoperatively due to an acute pulmonary embolism. There was a significant difference in hospitalization days between the 2 groups ($P = 0.032$; Table 4).

DISCUSSION

The Western region of China has consistently exhibited a high prevalence of hepatolithiasis.[18] The majority of patients with hepatolithiasis typically seek medical intervention only when they present with severe symptoms, thereby leading to a considerable escalation in the complexity of surgical procedures required. These cases often entail a combination of interventions, such as partial hepatectomy, biliary tract reconstruction, and choledoenteroanastomosis.[19] However, the occurrence of postoperative recurrence or residual stones has long been a vexing problem for hepatobiliary surgeons.

TABLE 1. Baseline Characteristics of the Fluorescence and Nonfluorescence Groups

Characteristics	Nonfluorescent group (N = 88) (mean ± SD)	Fluorescent group (N = 26) (mean ± SD)	*P*
Sex, n (%)			0.562
Male	39 (44.32)	10 (38.46)	
Female	49 (55.68)	16 (61.54)	
Age, (y)	51.8 ± 4.86	53.9 ± 5.02	0.129
The maximum diameter of the extrahepatic bile duct (mm)	15.23 ± 4.41	14.67 ± 5.29	0.924
White blood cell count	4.86 ± 1.83	5.09 ± 2.04	0.768
ALT (U/L)	87.53 ± 29.61	89.01 ± 24.25	0.942
AST (U/L)	61.47 ± 19.38	59.94 ± 25.81	0.732
TB (μmol/L)	39.73 ± 9.29	36.85 ± 11.02	0.862
DB (μmol/L)	31.93 ± 10.02	34.16 ± 9.53	0.979

ALT indicates alanine aminotransferase; AST, aspartate aminotransferase; DB, direct bilirubin; TB, total bilirubin.

TABLE 3. Intraoperative Conditions of the Patients in the Fluorescence and Nonfluorescence Groups

	Nonfluorescent group (N = 88)	Fluorescent group (N = 26)	*P*
The nature of the operation, n (%)			
LCBDE	37 (42.04)	16 (61.54)	0.2921
LCDJ	32 (36.36)	6 (23.08)	0.531
Re-LCDJ	19 (21.59)	4 (15.38)	0.893
The duration of surgery (min)	153.83 ± 56.97	127.64 ± 26.27	0.538
The bile duct identification time (min)*	39 ± 26.42	25 ± 12.27	0.036
The estimation of intraoperative blood loss (mL)	123.16 ± 97.29	90.87 ± 62.95	0.535
Conversion rate of laparotomy, n (%)	1 (1.14)	1 (3.84)	0.062

*$P < 0.05$.

Many patients have to undergo multiple surgeries, which can cause significant psychological and physical harm.

Recently, the laparoscopic technique has gained considerable traction in China. Previously, reoperation was considered a relative contraindication for laparoscopic surgery.[1–3] However, with the application and advancement of laparoscopic technology and choledochoscopy, a history of biliary and epicontinal surgeries has not been considered absolute contraindications of laparoscopic procedures.[20–22] In select cases, repeat laparoscopic surgery can still be performed. The primary challenge in laparoscopic biliary tract surgery lies in accurately identifying the biliary tract and effectively preventing any potential injuries to it.[6] However, determining the need for repeat biliary surgery can often be challenging due to factors such as hilar deformation, biliary scar formation, and recurrent biliary tract infections resulting from previous operations.[7] By utilizing the operator's tactile perception in an open state, intrabiliary stones and biliary stenosis can be utilized to enhance the recognition and facilitate identification of the biliary tract. Effectively and safely identifying the biliary tract is a crucial concern for most hepatobiliary surgeons.

Our study participants comprised patients who had undergone elective surgery for the biliary tract. A retrospective comparative study was conducted based on the utilization of a fluorescence imaging system, and the findings revealed no significant differences between the fluorescent and nonfluorescent groups in terms of operative time and intraoperative blood loss. However, significant differences were observed in the intraoperative biliary tract identification time. The study results also revealed a significant difference in the intraoperative biliary duct recognition rate in the fluorescent group (nonfluorescent group: 39 ± 26.42 vs. fluorescent group: 25 ± 12.27; $P = 0.036$). However, this outcome did not align with our initial expectations. The subsequent analysis indicated that the determination of the biliary duct recognition rate in this study was based on subjective criteria. Currently, there is no existing literature that precisely defines biliary duct recognition. Our research team has defined intraoperative biliary duct recognition time as the duration from the release of hilar adhesion to the confirmation of the biliary duct through puncture. However, in practical applications, the fluorescence imaging technique enables visualization of a part of the bile duct upon entering the abdominal cavity by activating the fluorescence mode. Continuous fluorescence imaging facilitates easier identification and separation of surrounding tissues around the bile duct. In the absence of fluorescence imaging, surgeons often rely on anatomic landmarks to determine the precise location of the bile duct, thereby prolonging the identification time. After comparing the data, we also observed that, although there was no statistically significant difference in the operative time between the 2 groups (nonfluorescent group: 153.83 ± 56.97 vs. fluorescent group: 127.64 ± 26.27; $P = 0.538$), a significant difference in the postoperative hospitalization days was observed (nonfluorescent group: 10.35 ± 2.87 vs. fluorescent group: 7.13 ± 1.23; $P = 0.032$). The easier identification of the bile duct with the assistance of fluorescence imaging technology can potentially lead to a reduced risk of damaging the surrounding tissues during reoperation, thereby potentially shortening the patients' hospital stay. It is interesting to note that in this study, although the fluorescence group demonstrated a shortened bile duct identification time, they did not show a reduction in the laparotomy conversion rate. In the fluorescence group, 1 patient required conversion to laparotomy due to severe gastric antrum and hepatic hilar adhesion after partial bile duct identification using fluorescence imaging. The observed phenomenon may be attributed to the fact that the patients included in this study had previously undergone biliary tract surgery.

TABLE 4. Postoperative Condition of the Patients in the Fluorescence and Nonfluorescence Groups

	Nonfluorescent group (N = 88)	Fluorescent group (N = 26)	*P*
Intestinal function recovery (d)	1.31 ± 0.1	1.27 ± 0.5	0.492
The duration of hospitalization after surgery*	9.89 ± 2.87	7.09 ± 1.11	0.032
Postoperative bile leakage, n (%)	2	2	1.872
Postoperative residual stones, n (%)	0	0	0.000
Postoperative complications Clavein-Dindo grade			0.679
I	8	3	
II	4	1	
III	1	0	
IV	0	0	
V	0	0	

*$P < 0.05$.

Specifically, the present study included 5 cases of open choledoenterostomy and 3 cases of open pancreaticoduodenectomy. These patients frequently presented with severe hepatic portal adhesions resulting from previous surgeries. In particular instances, the technique of encircling the gastroduodenal artery with the round ligament of the liver increases the risk of developing significant hepatic portal adhesion, necessitating conversion to laparotomy. We suggest that the decision to adopt laparoscopy for these patients should be made based on a comprehensive evaluation of the surgeon's operative experience and the level of teamwork of the involved medical professional rather than pursuing minimally invasive procedures without considering other factors. We also found no statistically significant differences in the postoperative ventilation, bile leakage, and stone recurrence rates at 6 months after surgery between the 2 groups ($P > 0.05$).

Previous studies on ICG imaging in hepatobiliary surgery primarily focused on laparoscopic cholecystectomy and liver tumor resection,[23] yielding a plethora of diverse suggestions for ICG application. The most commonly recommended approach is to administer 2.5 mg of ICG intravenously at 2 hours before surgery, coinciding with the peak concentration of ICG in the bile.[24] A recent meta-analysis demonstrated that administering 5 mg of ICG intravenously at least 3 hours before fluorescence imaging resulted in the clear visualization of intraoperative bile ducts.[25] Directly injecting a diluted solution of ICG (~0.025 mg/mL) into the bile duct following intraoperative biliary puncture has been reported to enhance the binding affinity between ICG and protein, as this concentration maximizes the fluorescence intensity of ICG.[23] In the present study, considering that all patients had previously undergone gallbladder removal and most of them presented with varying degrees of biliary obstruction, the injection time for ICG was determined to be 60 minutes before the operation to prevent suboptimal visualization of the biliary tract caused by either early or delayed ICG injection. However, in practical application, we encountered significant challenges in determining the optimal imaging intensity of ICG. This is because the ICG imaging system operates similarly to a GPS system, where the optimal imaging intensity can be likened to the broadcasting system within the GPS framework. Currently, there is a lack of standardized criteria for determining biliary tract fluorescence imaging. In most clinical studies, the evaluation of intraoperative fluorescence imaging relies on subjective visual assessment by surgeons, resulting in significant interobserver variability.[26] One crucial aspect that needs to be addressed in ICG fluorescent-guided surgery is the necessity to quantify the fluorescence signals to ensure enhanced clinical decision-making. This limitation can be overcome by identifying unique reporting criteria and establishing objective fluorescence thresholds based on fluorescence signal patterns. This is an active area of research, with an ongoing development of specialized software algorithms for digital imaging analysis.[23–25] The current systems have undergone preclinical testing, but they still require complete validation and eventual integration with existing laparoscopic instruments. This has the potential to yield significant outcomes in standardizing clinical trials, particularly in the field of perfusion assessment.[27] In the present study, there were 5 patients who had previously undergone bilioenterostomy and were now diagnosed with anastomotic stones, but no imaging data were obtained from these patients. Although intraoperative fluorescence imaging of the liver was attempted, the procedure failed due to the presence of adhesion at the bilioenterostomy site and considerable stone incarceration after anastomosis. Further investigation is needed to determine safe and efficient methods for visualizing the bile duct in such patients.

The present study has a major limitation. The study design has an observational and retrospective nature. Due to the limited availability of fluorescence laparoscopic imaging equipment in our hospital (only 2 sets of equipment were available), conducting a prospective randomized controlled study has proven challenging, resulting in a significant bias. Nevertheless, this study still offers valuable insights that are useful in clinical practice.

In summary, the application of ICG fluorescence imaging technology in repeat biliary tract surgery enables early intraoperative identification of the biliary tract, thereby reducing the operative time and minimizing the risk of injury to nonoperative areas. The utilization of this technique enhances the visualization of the biliary tract system, thereby mitigating the risk of inadvertent intraoperative damage caused by insufficient identification.

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