Utility of fluorescent cholangiography during laparoscopic cholecystectomy: A systematic review

Antonio Pesce, Gaetano Piccolo, Gaetano La Greca, Stefano Puleo

Antonio Pesce, Gaetano La Greca, Stefano Puleo, Department of Medical and Surgical Sciences and Advanced Technologies “G.F. Ingrassia”, University of Catania, 95123 Catania, Italy

Gaetano Piccolo, Department of Surgery, University of Catania, 95123 Catania, Italy

Author contributions: Pesce A designed the research; Piccolo G performed the research; Pesce A and Piccolo G analyzed the data; Pesce A and Piccolo G wrote the paper; La Greca G and Puleo S supervised the paper; all authors read and approved the final manuscript.

Conflict-of-interest statement: All the authors declare that they have no competing interests.

Data sharing statement: The technical appendix, statistical code, and dataset are available from the corresponding author at nino.fish@hotmail.it.

Open-Access: This article is an open-access article which was selected by an in-house editor and fully peer-reviewed by external reviewers. It is distributed in accordance with the Creative Commons Attribution Non Commercial (CC BY-NC 4.0) license, which permits others to distribute, remix, adapt, build upon this work non-commercially, and license their derivative works on different terms, provided the original work is properly cited and the use is non-commercial. See: http://creativecommons.org/licenses/by-nc/4.0/

Correspondence to: Antonio Pesce, MD, Department of Medical and Surgical Sciences and Advanced Technologies “G.F. Ingrassia”, University of Catania, Via S. Sofia 84, 95123 Catania, Italy. nino.fish@hotmail.it

Telephone: +39-32-86680943
Fax: +39-0953782912

Received: February 4, 2015
Peer-review started: February 6, 2015
First decision: March 10, 2015
Revised: April 16, 2015
Accepted: May 27, 2015
Article in press: May 27, 2015
Published online: July 7, 2015

Abstract

AIM: To verify the utility of fluorescent cholangiography for more rigorous identification of the extrahepatic biliary system.

METHODS: MEDLINE and PubMed searches were performed using the key words “fluorescent cholangiography”, “fluorescent angiography”, “intraoperative fluorescent imaging”, and “laparoscopic cholecystectomy” in order to identify relevant articles published in English, French, German, and Italian during the years of 2009 to 2014. Reference lists from the articles were reviewed to identify additional pertinent articles. For studies published in languages other than those mentioned above, all available information was collected from their English abstracts. Retrieved manuscripts (case reports, reviews, and abstracts) concerning the application of fluorescent cholangiography were reviewed by the authors, and the data were extracted using a standardized collection tool. Data were subsequently analyzed with descriptive statistics. In contrast to classic meta-analyses, statistical analysis was performed where the outcome was calculated as the percentages of an event (without comparison) in pseudo-cohorts of observed patients.

RESULTS: A total of 16 studies were found that involved fluorescent cholangiography during standard laparoscopic cholecystectomies (n = 11), single-incision robotic cholecystectomies (n = 3), multiport robotic cholecystectomy (n = 1), and single-incision laparoscopic cholecystectomy (n = 1). Overall, these preliminary studies indicated that this novel technique was highly sensitive for the detection of important biliary anatomy and could facilitate the prevention of bile duct injuries. The structures effectively identified before dissection of Calot’s triangle included the cystic duct (CD), the common hepatic duct (CHD), the common bile duct (CBD), and the CD-CHD junction. A review of the literature revealed that the frequencies
of detection of the extrahepatic biliary system ranged from 71.4% to 100% for the CD, 33.3% to 100% for the CHD, 50% to 100% for the CBD, and 25% to 100% for the CD-CHD junction. However, the frequency of visualization of the CD and the CBD were reduced in patients with a body mass index > 35 kg/m² relative to those with a body mass index < 35 kg/m² (91.0% and 64.0% vs. 92.3% and 71.8%, respectively).

CONCLUSION: Fluorescent cholangiography is a safe procedure enabling real-time visualization of bile duct anatomy and may become standard practice to prevent bile duct injury during laparoscopic cholecystectomy.

Key words: Extrahepatic biliary system; Laparoscopic cholecystectomy; Bile duct injury; Biliary anomalies; Fluorescent cholangiography

© The Author(s) 2015. Published by Baishideng Publishing Group Inc. All rights reserved.

Core tip: Fluorescent cholangiography (FC) is a safe and effective novel procedure that enables real-time visualization of the biliary system. Intraoperative FC has been successfully performed during minimally invasive cholecystectomies in various studies, including standard laparoscopic cholecystectomies, single incision cholecystectomies, and robotic cholecystectomies. The primary aim of this review is to verify the utility of this technique for more rigorous identification of the extrahepatic biliary system in order to prevent bile duct injuries intraoperatively. The second aim is to illuminate potential benefits and limitations in the application of FC.

INTRODUCTION

Laparoscopic cholecystectomy (LC) is one of the most commonly performed surgical procedures worldwide. Annually, more than 750,000 procedures are performed in the United States[1] and approximately 60,000 in Japan[2]. Bile duct injury (BDI) is a rare but very serious complication of LC, with an incidence of 0.3%–0.7%[3–7] and a significant impact on quality of life and overall survival[8].

The high frequency of BDI with laparoscopic cholecystectomy was first considered to be a consequence of the initial learning curve of the surgeon, but it later became clear that the primary cause of BDI was misinterpretation of biliary anatomy (71%–97% of all cases)[9]. Intraoperative cholangiography (IOC) has been advised by many authors as the technique reduces the risk of BDI[10]. However, the procedure also has inherent limitations and is therefore reserved for select cases[11,12]. Moreover, worldwide consensus regarding the implementation of IOC is still lacking[13].

Hepatobiliary surgery has become increasingly safe as a result of considerable progress in equipment, technology, perioperative management, and surgical technique. Fluorescent cholangiography (FC) is a novel approach, which offers real-time intraoperative imaging of the biliary anatomy. The first intraoperative use of FC in humans was described by Ishizawa et al[14] in 2010. The method involves the administration of indocyanine green (ICG) by either intrabiliary injection or intravenous injection 30 min before surgery. ICG binds to proteins present in bile and is excreted exclusively by the liver when administered intravenously. The excitation of protein-bound ICG by near-infrared light causes it to fluoresce, thereby delineating components of the biliary system for the surgeon. Fluorescence and imaging is achieved through a system consisting of a small control unit, a charge-coupled device camera, a xenon light source, and a 10 mm laparoscope containing specially coated lenses that transmit near-infrared light.

Intraoperative FC has been successfully performed during minimally invasive cholecystectomies in various studies, including standard LCs, single-incision cholecystectomies (SILCs), and robotic cholecystectomies (RCs)[15–34]. The primary aim of this review was to verify the utility of this technique for the intraoperative visualization of the extrahepatic biliary system in order to reduce the incidence of BDIs. The second aim was to illuminate the potential benefits and relative limitations of intraoperative FC.

MATERIALS AND METHODS

Literature search

MEDLINE and PubMed searches were performed using the key words “fluorescent cholangiography”, “fluorescent angiography”, “intraoperative fluorescent imaging”, and “laparoscopic cholecystectomy” in order to identify relevant articles published in English, French, German, and Italian from 2009 to 2014. Reference lists from the articles were reviewed to identify additional relevant articles. For studies published in languages other than those mentioned above, all available information was taken from their English abstracts. All studies that contained material applicable to the topic were considered. Retrieved manuscripts (case reports, reviews, and abstracts) were reviewed by the authors, and the data were extracted using a standardized collection tool. Data were analyzed using descriptive statistics.

Statistical analysis

In contrast to classic meta-analyses, the outcome is defined here as the percentages of an event (without comparison) in pseudo-cohorts of observed
patients. Overall proportions can be estimated from the weighted mean of percentages measured in each study. The weight in this case is derived from the number of subjects included in the study out of the total number of subjects in all studies, which is inverse of the variance in the classic meta-analyses. The confidence interval is calculated through the use of the normal distribution to approximate the binomial probabilities given that the condition “product of the probability and sample size ($np$) is more than 5” is fulfilled.

**RESULTS**

*Identification of biliary system with FC*

At the time of this review, a total of 16 studies were found which involved FC during standard LCs ($n = 11$), single-incision RCs (SIRC; $n = 3$), multiport RCs ($n = 1$), and SILC ($n = 1$).

The detection rates of major extrahepatic biliary structures with FC during laparoscopic or robotic cholecystectomy before dissection of Calot’s triangle are summarized in Table 1. Overall, the potential of this novel technique for the detection of important biliary anatomy was revealed in these preliminary studies. The structures successfully identified before dissection of Calot’s triangle included the cystic duct (CD), the common hepatic duct (CHD), the common bile duct (CBD), and the CD-CHD junction. A review of the literature revealed that the rates of detection of extrahepatic biliary system with this strategy ranged from 71.4% to 100% for CD, 33.3% to 100% for CHD, 50.0% to 100% for CBD, and 50.0% to 100% for the CD-CHD junction, with weighted averages of 96.2%, 78.1%, 72.0%, and 86.0%, respectively (Table 1).

Daskalaki et al.\[^{[19]}\] published the largest series to date of RCs performed with ICG fluorescence for the visualization of the biliary tree anatomy. Visualization of at least one biliary structure was possible in 99% of cases, whereas all four main structures were detected (CD, CBD, CHD, and CD-CHD junction) in 83% of cases. No major complications, including biliary injury or conversion to open or laparoscopic approach, occurred in this series.

Using near-infrared FC (NIRF-C), Osayi et al.\[^{[18]}\] reported rates of visualization of the CD, CBD, and CHD after complete dissection of Calot’s triangle of 95.1%, 76.8%, and 69.5%, respectively, compared to 72.0%, 75.6%, and 74.3% for IOC. In general, biliary structures were successfully identified with NIRF-C without biliary injuries or other major complications in 80% of cases.

These data indicated that FC provided a reliable roadmap of the bile duct anatomy, enabling surgeons to avoid BDIs while dissecting Calot’s triangle.

*Identification of biliary structures with FC before and after Calot’s dissection*

A review of the literature revealed that a preliminary dissection of Calot’s triangle led to an overall increase in the identification of all biliary structures. Ishizawa et al.\[^{[14]}\] in 2010 reported results on the first large cohort of patients ($n = 52$) who had undergone LC with ICG FC. Rates of visualization for the CD and the CHD were found to be 100% and 96% before dissection and 100% after dissection for both structures. Buchs et al.\[^{[21]}\] concurrently published preliminary results on a series of 12 SIRC cases performed with intraoperative ICG FC. The rates of visualization for the CD, CBD, and the CD-CHD junction before Calot’s dissection were 91.7%, 33.3%, 50.0%, and 25.0%, and 100.0%, 66.0%, 83.3%, and 58.0% after Calot’s dissection, respectively. More recently, Spinoglio et al.\[^{[22]}\] reported more encouraging data based on results from a cohort of patients ($n = 45$) who had undergone SIRC performed with routine ICG FC to evaluate the

### Table 1 Detection rates of biliary and vascular structures using fluorescent cholangiography $n$ (%)

| Ref.                             | Technique | $n$  | CD (%) | CHD (%)  | CD-CHD junction (%) | CBD (%) | CA       |
|----------------------------------|-----------|------|--------|----------|---------------------|---------|----------|
| Ishizawa et al.\[^{[14]}\]       | LC        | 35   | 35 (100)| 35 (100) | 35 (100)            | 35 (100) | 29 (83.0) |
| Daskalaki et al.\[^{[19]}\]      | RC        | 184  | 180 (97.8)| 173 (94.0)| 154 (83.6)        | 177 (96.1)| -        |
| Dip et al.\[^{[26]}\]            | LC        | 45   | 44 (97.7) | 27 (60.0) | -                   | 36 (80.0) | -        |
| Osayi et al.\[^{[18]}\]          | LC        | 82   | 78 (95.1) | 57 (69.5) | 63 (76.8)          | 63 (76.8) | -        |
| Dip et al.\[^{[26]}\]            | LC        | 43   | 42 (97.6) | 25 (58.1) | -                   | 34 (79.1) | -        |
| Verbeek et al.\[^{[21]}\]        | LC        | 14   | 14 (100)  | -        | -                   | -        | -        |
| Buchs et al.\[^{[21]}\]          | SIRC      | 23   | 23 (100)  | -        | -                   | -        | -        |
| Spinoglio et al.\[^{[22]}\]      | SIRC      | 45   | 42 (93.0) | 40 (80.0) | 40 (80.0)          | 41 (91.0) | -        |
| Schols et al.\[^{[26]}\]         | LC        | 15   | 15 (100)  | -        | -                   | 15 (100)  | -        |
| Buchs et al.\[^{[21]}\]          | SIRC      | 12   | 11 (91.7) | 4 (33.3)  | 3 (25.0)           | 6 (50.0)  | -        |
| Kaneko et al.\[^{[26]}\]         | LC        | 28   | 26 (92.9) | 27 (96.4) | -                   | -        | 25 (89)  |
| Ishizawa et al.\[^{[14]}\]       | SILC      | 7    | 5 (71.4)  | 7 (100)  | 7 (100)            | -        | 4 (57.1) |
| Aoki et al.\[^{[32]}\]           | LC        | 14   | 10 (71.4) | -        | -                   | 10 (71.4) | -        |
| Ishizawa et al.\[^{[14]}\]       | LC        | 52   | 52 (100)  | 50 (96.2) | 50 (96.2)          | -        | -        |
| Ishizawa et al.\[^{[14]}\]       | LC        | 1    | 1 (100)   | 1 (100)  | 1 (100)            | -        | -        |

Weighted average, % (95%CI)

| Detected structure | n | CD | CHD | CD-CHD junction | CBD | CA       |
|--------------------|---|----|-----|-----------------|-----|----------|
| CD                 | n | 78.1% | 72.0% | 86.0%          |      |          |
| CHD                | n | 80.0% | 76.8% | 69.5%          |      |          |
| CBD                | n | 91.7% | 66.0% | 83.3%          |      |          |
| CD-CHD junction    | n | 96.0% | 75.6% | 74.3%          |      |          |

CA: Cystic artery; CBD: Common bile duct; CD: Cystic duct; CHD: Common hepatic duct; LC: Standard laparoscopic cholecystectomy; RC: Robotic cholecystectomy; SILC: Single-incision laparoscopic cholecystectomy; SIRC: Single-incision robotic cholecystectomy.
extrahepatic biliary anatomy. The visualization rates of the CD, CHD, and CBD before the dissection of Calot’s triangle were 93%, 88%, and 91%, respectively. After dissection of Calot’s triangle, all of the rates increased to 97%. Statistical analysis confirmed that the increases in visualization rates from all studies were statistically significant (Table 2).

**Identification of biliary structures with FC in obese patients**

Although FC during LC appears to be a safe and effective procedure enabling real-time visualization of the biliary duct anatomy, limited results have been reported for when patients present with more challenging clinical conditions, such as obesity or acute cholecystitis. One of the potential limiting factors of the procedure is that near-infrared light has a penetration capability of only 5-10 mm. Therefore, the identification of the Calot’s triangle structures can be challenging, especially in cases where there is an abundance of fatty tissue or severe inflammation of the gallbladder and surrounding tissues. In a cohort of obese patients[^19^], the CD, CHD, and CBD were successfully identified with ICG fluorescence in 97%, 94%, and 95% of the cases, respectively, and the CD-CHD junction in 82% of the cases. However, some differences between patients were reported based on a body mass index (BMI) > 30 kg/m^2 or < 30 kg/m^2[^19^].

NIRF-C was also used to evaluate the extrahepatic biliary structures, before and after complete dissection of Calot’s triangle, in patients (n = 82) who had undergone elective LC[^18^]. A number of obese patients were also included (39/82; 47.6%[^18^]), and the results were compared to the routine use of IOC.A modestly improved rate for the identification of biliary structures was observed in patients with BMI < 30 kg/m^2 (43/82; 52.4%) relative to those with BMI > 30 kg/m^2. Only a statistical difference for the visualization of the CD-CHD junction emerged (24.4% vs 76.8%, P = 0.04). However, the rates of visualization of the CD and the CBD were decreased in patients with a BMI > 35 kg/m^2 (22/82; 26.8%) relative to patients with a BMI < 35 kg/m^2 (91.0% and 64.0% vs 92.3% and 71.8%, respectively). Finally, in the case with the highest BMI (63 kg/m^2), the only structure visualized was the CD.In all patients, the CD was visualized at a significantly higher rate with NIRF-C than IOC (95.1% vs 72.0%, P < 0.001), while there was no difference in visualization of the CD in the subgroup of patients (n = 62) who had undergone both NIRF-C and IOC (98.4% vs 95.2%).

Overall, few results regarding the use of FC in obese patients have been reported.According to the data available, no statistically significant difference exists between patients with BMI < 30 kg/m^2 compared to patients with BMI > 30 kg/m^2, regarding improved visualization of the biliary structures. The visualization frequency of the biliary structures in obese relative to non-obese patients, ranges from 92.3% to 100% vs 90.0% to 98.7% for the CD, 61.5% to 94.0% vs 40.0% to 93.9% for the CHD, and 50.0% to 95.0% vs 50.0% to 97.5% for the CBD, respectively (Table 3). There was an apparent difference only with regard to the visualization of the CD-CHD junction (61.0% to 82.3% vs 76.7% to 85.3%, respectively).

**Identification of biliary structures with FC in patients with cholecystitis**

Data were analyzed in the patients presenting with a second complicating clinical factor, cholecystitis, excluding patients with acute and gangrenous cholecystitis undergoing emergency surgery. Even in this subset of challenging cases, the successful identification of the CD, CHD, and CBD and the CD-CHD junction was reported to be 91.6%, 79.1%, 79.1%, and 75.0%, respectively[^19^]. Similar results for visualization rates in such patients have been reported in a second study: 94.5%, 57.0%, and 72.0% for the CD, CHD, and CBD respectively[^20^] (Table 4). The number of patients examined, however, was too small for conclusive determination of the utility of FC in patients with cholecystitis. For these patients, Dip et al[^20^] has advocated for the combined
use of FC to identify the CD, followed by IOC to verify the CD-CHD junction. Preoperative magnetic resonance cholangiopancreatography (MRCP) offers an alternative to this strategy. In addition to excluding the concomitant lithiasis of the CBD, MRCP imaging allows for accurate visualization of the intra- and extrahepatic biliary tracts and can reveal a greater number of primary or secondary anatomical variations due to acute inflammation.

Detection of biliary stones
One of the important applications of standard fluoroscopic IOC is for the detection of biliary stones. To date, there is no evidence that FC can effectively identify CBD stones. However, the ability of this technique to detect stones elsewhere in the biliary tree has not been thoroughly investigated. Currently, results do not support the replacement of standard IOC with FC in cases where biliary stones are suspected preoperatively. Biliary stones in the cystic duct observed in preoperative cholangiography were correctly diagnosed in four patients with fluoroscopic IOC [14]. The fluorescent images were helpful for determining the optimal point for dividing the cystic duct without leaving stones in the remaining cystic duct. In contrast, FC failed to detect CBD stones diagnosed before surgery in one patient. According to Daskalaki et al [19], FC could help to reveal a dilation or gallstones in the CD, but the method cannot exclude the presence of CBD stones.

Detection of the biliary anomalies and leaks
The ability to detect biliary anomalies with FC has been investigated. Accessory bile ducts were diagnosed before surgery by drip infusion cholangiography and/or MRCP in 8/52 (15%) patients [14]; a right lateral, right paramedian, or a left paramedian sector branch were all draining directly into the CHD. In two patients, the accessory bile duct was detected with FC before dissection of Calot’s triangle. In the remaining six patients, the accessory bile duct was observed only after dissection of Calot’s triangle. Fluorescent imaging also revealed communicating accessory bile ducts between the left and right lobes of the liver in two patients. Anatomical variations were also identified with FC in an additional five patients (2.7%) [19]. In two cases, the CD was joined directly to the right hepatic duct, while in a third, the CBD was completely posterior to the hepatic artery. A fourth patient had an extended CD that was observed running parallel to the right hepatic duct before joining the CBD, and the last patient presented with an aberrant canaliculus from liver segment VI to the CHD.

The ability to detect intraoperative bile leaks with FC has been investigated to a limited extent. Bile leakage caused by cannulation of the CD in humans during IOC was easily visualized with fluorescent imaging [35]. However, detection of previously unknown bile leaks has not been reported.

Fluorescent angiography concomitant with cholangiography
Coupling of the fluorescent angiography with cholangiography has been described to enable identification of the cystic artery [14,25]. A second intraoperative bolus injection of ICG was required, however. In the largest study, the cystic artery began to fluoresce 20 to 30 seconds after the bolus, and it was identified in 25/28 (89.3%) patients [25]. In two additional studies, the cystic artery was successfully localized in 57% [14].

Table 3  Identification of biliary structures using fluorescent cholangiography in obese patients

| Vascular structure | Daskalaki et al [19] | Osayi et al [18] | Buchs et al [24] | Weighted average, % (95%CI) |
|--------------------|---------------------|------------------|------------------|-----------------------------|
|                    | n/total             | n/total          | n/total          | n/total                     |
| CD                 | BMI > 30 kg/m²      |                  |                  |                             |
| CD                 | 99/102              | 36/39            | 2/2              | 95.8 (92.5-99.0)            |
| CHD                | 96/102              | 24/39            | 0/2              | 83.9 (80.8-87.8)            |
| CBD                | 97/102              | 28/39            | 1/2              | 88.0 (83.1-93.0)            |
| CD-CHD junction    | 84/102              | 26/39            | 0/2              | 76.9 (70.2-83.5)            |
| CD                 | 81/82               | 42/43            | 9/10             | 97.1 (94.6-99.5)            |
| CHD                | 77/82               | 33/43            | 4/10             | 84.4 (78.8-90.0)            |
| CBD                | 80/82               | 35/43            | 5/10             | 88.9 (84.0-93.7)            |
| CD-CHD junction    | 70/82               | 37/43            | 3/10             | 81.4 (75.3-87.5)            |

BMI: Body mass index; CBD: Common bile duct; CD: Cystic duct; CHD: Common hepatic duct.

Table 4  Identification of biliary structures using fluorescent cholangiography in patients with acute cholecystitis

| Vascular structure | Daskalaki et al [19] | Dip et al [30] |
|--------------------|---------------------|----------------|
|                    | n/total             | n/total        |
| CD                 | 22/24               | 91.6           |
| CHD                | 19/24               | 79.1           |
| CBD                | 19/24               | 79.1           |
| CD-CHD junction    | 18/24               | 75.0           |

CBD: Common bile duct; CD: Cystic duct; CHD: Common hepatic duct.
and 83%\(^\text{17}\) of cases.

**DISCUSSION**

FC has several potential advantages over conventional radiographic IOC. First, FC saves time, and second, FC prevents BDIs typically associated with a conventional IOC approach. Third, the technique is more convenient, as it requires only a preoperative intravenous ICG injection, and fluorescent images of the biliary tract are obtained in real time at any point during surgery without the assistance of radiation technicians. Fourth, fluorescent imaging enables surgeons to evaluate the extrahepatic biliary system easily and within a short timeframe. Lastly, the procedure is safe. There is no exposure to radiation, and the risk of adverse reactions to the ICG injection is very small (about 0.003% at doses exceeding 0.5 mg/kg\(^\text{35}\)). In short, ten characteristics have been highlighted for the use of FC in LC over IOC: feasibility, cost (cheaper), operating time (faster), specificity, instructional applications, safety, lack of learning curve, lack of X-ray exposure, simplicity, and real-time surgery.\(^\text{20}\)

FC, however, also has some inherent deficiencies, namely, the limited tissue penetration of near-infrared light. Limited penetration of light results in the inability to visualize deep intrahepatic ducts or extrahepatic ducts obscured by surrounding organs and tissue. Practically, the technique is severely limited in patients with specific clinical conditions, such as obesity and cholecystitis, due to obstruction of near-infrared light.

In conclusion, ICG FC is a safe and effective procedure that enables real-time visualization of the biliary system. For these reasons, this novel procedure may become standard practice in order to prevent bile duct injuries. Moreover, the technique may become standard practice in order to prevent bile duct injuries.

**ACKNOWLEDGMENTS**

The authors would like to thank Dr. John Justin Rizzo, Adjunct Professor at University of Catania, Department of Foreign Languages, for his help in revising this paper, and Marine Castaing, MSc, at the Department of Medical and Surgical Sciences "G.F. Ingrassia", University of Catania, for help with statistical analysis.

**REFERENCES**

1. Flum DR, Dellinger EP, Cheadle A, Chan L, Koepsell T. Intraoperative cholangiography and risk of common bile duct injury during cholecystectomy. *JAMA* 2003; 289: 1639-1644 [PMID: 12672731 DOI: 10.1001/jama.289.13.1639]

2. Ministry of Health, Labour and Welfare of Japan. Prospective 3-year study of 10,174 patients. Swiss Association of Laparoscopic and Thoracoscopic Surgery. *Surg Endosc* 1998; 12: 1303-1310 [PMID: 9788582 DOI: 10.1007/s004649900486]

3. Fletcher DR, Hobbs MS, Tan P, Valinsky LJ, Hockey RL, Pikora TJ, Knuijman MW, Sheiner HJ, Edis A. Complications of laparoscopic cholecystectomy in Switzerland. A prospective 3-year study of 10,174 patients. Swiss Association of Laparoscopic and Thoracoscopic Surgery. *Surg Endosc* 1998; 12: 1303-1310 [PMID: 9788582 DOI: 10.1007/s004649900486]

4. Z’graggen K, Wéhrli H, Metzger A, Buehler M, Frei E, Klaiber C. Complications of laparoscopic cholecystectomy in Switzerland. A prospective study of 10,174 patients. Swiss Association of Laparoscopic and Thoracoscopic Surgery. *Surg Endosc* 1998; 12: 1303-1310 [PMID: 9788582 DOI: 10.1007/s004649900486]

5. Z’graggen K, Wéhrli H, Metzger A, Buehler M, Frei E, Klaiber C. Complications of laparoscopic cholecystectomy in Switzerland. A prospective study of 10,174 patients. Swiss Association of Laparoscopic and Thoracoscopic Surgery. *Surg Endosc* 1998; 12: 1303-1310 [PMID: 9788582 DOI: 10.1007/s004649900486]

6. Waage A, Nilsson M. Iatrogenic bile duct injury: a population-based study of 152 776 cholecystectomies in the Swedish Inpatient Registry. *Arch Surg* 2006; 141: 1207-1213 [PMID: 17179893 DOI: 10.1001/archsurg.141.12.1207]

7. Japanese Society for Endoscopic Surgery. The 9th Questionnaire Survey. Accessed 26 June 2009. Available from: URL: http://www.annals.org/holding/2009/jsep090601.html

**COMMENTS**

**Background**

Intraoperative cholangiography has been advised by many authors, as it reduces the risk of bile duct injury. However the technique has inherent limitations and is therefore generally reserved for select cases. Moreover, worldwide consensus regarding the implementation of intraoperative cholangiography is still lacking. Fluorescent cholangiography (FC) is a safe and effective novel procedure that enables real-time visualization of the biliary system. The primary aim of this review is to verify the utility of this technique for more rigorous identification of the extrahepatic biliary system in order to reduce bile duct injuries intraoperatively. The second aim is to illuminate the limitations of the procedure as well as the potential benefits.

**Research frontiers**

The first intraoperative use of FC in humans was described by Ishizawa et al in 2010. The method involves the administration of indocyanine green (ICG) by either intrabiliary injection or intravenous injection 30 min before surgery. ICG binds to proteins present in bile and is excreted exclusively by the liver when administered intravenously. The excitation of protein-bound ICG by near-infrared light causes it to fluoresce, thereby delineating components of the biliary system for the surgeon. A fluorescent imaging system consisting of a small control unit, a charge-coupled device camera, a xenon light source, and a 10 mm laparoscope containing specially coated lenses that transmit near-infrared light has been devised specifically for this surgical application.

**Innovations and breakthroughs**

Intraoperative FC has been successfully performed during mini-invasive cholecystectomies in various studies, including standard laparoscopic cholecystectomies, single incision cholecystectomies, and robotic cholecystectomies.

Retrieved manuscripts (case reports, reviews, and abstracts) concerning the utility of FC were reviewed by the authors, and the data were extracted using a standardized collection tool.

**Applications**

This review suggests that FC is a valid method to detect extrahepatic biliary anatomy during laparoscopic cholecystectomy, and that the technique may become standard practice in order to prevent bile duct injuries.

**Terminology**

FC is a novel method that involves the administration of ICG by either intrabiliary injection or intravenous injection 30 min before surgery, which is excited by a near-infrared light source, thus permitting visualization of the extrahepatic biliary system intraoperatively.

**Peer-review**

In this systematic review, the authors have presented a thorough and critical analysis of the utility of FC for more rigorous identification of biliary anatomy in order to prevent bile duct injury during laparoscopic cholecystectomies.
The case for selective cholangiography. Br J Surg 2006; 93: 158-168 [PMID: 16432812 DOI: 10.1002/bjs.5266]

Giovanni A. Identification of anomalous biliary anatomy using near-infrared fluoroscopic cholangiography. J Gastrointest Surg 2012; 16: 1814-1815 [PMID: 22752550 DOI: 10.1007/s11611-014-1945-2]

Bucchi NC. Indocyanine green in laparoscopic cholecystectomy: results of 252 cases from a human factors and cognitive psychology study. Surg Endosc 2011; 25: 2631-2636 [PMID: 21424202 DOI: 10.1007/s00464-011-1616-2]

Ishizawa T. Bandai Y, Hasegawa K, Kokudo N. Fluorescent cholangiography in laparoscopic cholecystectomy: an initial experience. J Surg 2009; 144: 381-382 [PMID: 19380655 DOI: 10.1001/archsurg.2009.9]

Ishizawa T. Bandai Y, Hasegawa K, Kokudo N. Fluorescent cholangiography during laparoscopic cholecystectomy: indocyanine green or new fluorescent agent? World J Surg 2010; 34: 2505-2506 [PMID: 20563724 DOI: 10.1007/s00268-010-0676-0]

Ishizawa T. Murakami M, Yasuda Y, Kusano K, Niiya T, Kato H, Murai N, Otsuka K, Kusano M, Kato T. Intraoperative fluorescent imaging using indocyanine green for liver mapping and cholangiography. J Hepatobiliary Pancreat Sci 2010; 17: 590-594 [PMID: 19846652 DOI: 10.1007/s00534-009-0197-0]

Pertesnislis D. Fluorescent indocyanine green for imaging of bile ducts during laparoscopic cholecystectomy. Arch Surg 2009; 144: 978 [PMID: 19841371 DOI: 10.1001/archsurg.2009.179]

Ishizawa T. Bandai Y, Kokudo N. Fluorescent cholangiography during laparoscopic cholecystectomy: a feasibility study on early biliary tract delineation. Surg Endosc 2013; 27: 1530-1536 [PMID: 23076461 DOI: 10.1007/s00464-012-2635-3]

Kanejo K, Ishizawa T, Masuda K, Kagawachi Y, Aoki T, Sakamoto Y, Hasegawa K, Sugawara Y, Kokudo N. Indocyanine green injection technique for use in fluorescent angiography concomitant with cholangiography during laparoscopic cholecystectomy. J Laparoendosc Adv Surg Tech A 2010; 20: 2631-2636 [PMID: 21424202 DOI: 10.1007/s00464-011-1616-2]

Ishizawa T, Bandai Y, Hasegawa K, Kokudo N. Fluorescent cholangiography in laparoscopic cholecystectomy: indocyanine green or new fluorescent agent? World J Surg 2010; 34: 2505-2506 [PMID: 20563724 DOI: 10.1007/s00268-010-0676-0]

Ishizawa T. Murakami M, Yasuda Y, Kusano K, Niiya T, Kato H, Murai N, Otsuka K, Kusano M, Kato T. Intraoperative fluorescent imaging using indocyanine green for liver mapping and cholangiography. J Hepatobiliary Pancreat Sci 2010; 17: 590-594 [PMID: 19846652 DOI: 10.1007/s00534-009-0197-0]

Ishizawa T. Murakami M, Yasuda Y, Kusano K, Niiya T, Kato H, Murai N, Otsuka K, Kusano M, Kato T. Intraoperative fluorescent imaging using indocyanine green for liver mapping and cholangiography. J Hepatobiliary Pancreat Sci 2010; 17: 590-594 [PMID: 19846652 DOI: 10.1007/s00534-009-0197-0]

Ishizawa T. Bandai Y, Kokudo N. Fluorescent cholangiography during laparoscopic cholecystectomy: indocyanine green or new fluorescent agent? World J Surg 2010; 34: 2505-2506 [PMID: 20563724 DOI: 10.1007/s00268-010-0676-0]

Ishizawa T. Murakami M, Yasuda Y, Kusano K, Niiya T, Kato H, Murai N, Otsuka K, Kusano M, Kato T. Intraoperative fluorescent imaging using indocyanine green for liver mapping and cholangiography. J Hepatobiliary Pancreat Sci 2010; 17: 590-594 [PMID: 19846652 DOI: 10.1007/s00534-009-0197-0]

Ishizawa T. Bandai Y, Kokudo N. Fluorescent cholangiography during laparoscopic cholecystectomy: indocyanine green or new fluorescent agent? World J Surg 2010; 34: 2505-2506 [PMID: 20563724 DOI: 10.1007/s00268-010-0676-0]

Ishizawa T. Bandai Y, Kokudo N. Fluorescent cholangiography during laparoscopic cholecystectomy: indocyanine green or new fluorescent agent? World J Surg 2010; 34: 2505-2506 [PMID: 20563724 DOI: 10.1007/s00268-010-0676-0]

Ishizawa T. Bandai Y, Kokudo N. Fluorescent cholangiography during laparoscopic cholecystectomy: indocyanine green or new fluorescent agent? World J Surg 2010; 34: 2505-2506 [PMID: 20563724 DOI: 10.1007/s00268-010-0676-0]

Ishizawa T. Bandai Y, Kokudo N. Fluorescent cholangiography during laparoscopic cholecystectomy: indocyanine green or new fluorescent agent? World J Surg 2010; 34: 2505-2506 [PMID: 20563724 DOI: 10.1007/s00268-010-0676-0]

Ishizawa T. Bandai Y, Kokudo N. Fluorescent cholangiography during laparoscopic cholecystectomy: indocyanine green or new fluorescent agent? World J Surg 2010; 34: 2505-2506 [PMID: 20563724 DOI: 10.1007/s00268-010-0676-0]
