Format for Manuscript Submission: Systematic Reviews

Name of journal: *World Journal of Gastroenterology*

Manuscript NO:

Manuscript Type: SYSTEMATIC REVIEWS

Utility of fluorescent cholangiography during laparoscopic cholecystectomy: A systematic review

Pesce A *et al.* Fluorescent cholangiography in laparoscopic cholecystectomy

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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.

Supported by

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Abstract

BACKGROUND

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/m^2 relative to those with a body mass index < 35 kg/m^2 (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: Bile duct injury; Biliary anomalies; Extrahepatic biliary system; Fluorescent cholangiography; Laparoscopic cholecystectomy

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 mini-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 750000 procedures are performed in the United States[1] and approximately 60000 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[1,4,6,10]. 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 mini-invasive cholecystectomies in various studies, including standard LCs, single-incision cholecystectomies (SILCs), and robotic cholecystectomies (RCs)[15,16–33]. 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 (SIRCs; 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 25.5% 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, CHD, CBD, 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*[22] concurrently published preliminary results on a series of 12 SIRC cases performed with intraoperative ICG FC. The rates of visualization for the CD, CHD, 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*[23] reported more encouraging databased on results from a cohort of patients (n = 45) who had undergone SIRC performed with routine ICG FC to evaluate the 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-Cwas 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 under gone 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% versus90.0% to 98.7% for the CD, 61.5% to 94.0% versus40.0% to 93.9% for the CHD, and 50.0% to 95.0% versus 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, 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[14,17,25,35]. 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] and 83%[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 (~0.003% at doses exceeding 0.5 mg/kg)[34]. 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[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 BDI during LC. Furthermore, the technique may replace RC as it allows for a more accurate and less invasive identification of the extrahepatic biliary anatomy tract, which reduces operative time, medical costs, and major postoperative complications[14,15]. Further research should aim to assess the impact of this technique on adverse events and long-term patient outcomes.

ACKNOWLEDGEMENTS

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**. Proceedings of Central Social Insurance Medical Council, 2008. Available from: URL: http: //www.mhlw.go.jp/shingi/2009/05/s0514-6.html [accessed 26 June 2009]

3 **Z'graggen K**, Wehrli H, Metzger A, Buehler M, Frei E, Klaiber C. 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: 9788852 DOI: 10.1007/s004649900846]

4 **Fletcher DR**, Hobbs MS, Tan P, Valinsky LJ, Hockey RL, Pikora TJ, Knuiman MW, Sheiner HJ, Edis A. Complications of cholecystectomy: risks of the laparoscopic approach and protective effects of operative cholangiography: a population-based study. *Ann Surg* 1999; **229**: 449-457 [PMID: 10203075 DOI: 10.1097/00000658-199904000-00001]

5 **Nuzzo G**, Giuliante F, Giovannini I, Ardito F, D'Acapito F, Vellone M, Murazio M, Capelli G. Bile duct injury during laparoscopic cholecystectomy: results of an Italian national survey on 56 591 cholecystectomies. *Arch Surg* 2005; **140**: 986-992 [PMID: 16230550 DOI: 10.1001/archsurg.140.10.986]

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: 17178963 DOI: 10.1001/archsurg.141.12.1207]

7 **Japan Society for Endoscopic Surgery**. The 9th Questionnaire Survey. Available from: URL: http: //www.med.oita-u.ac.jp/surgery1/JSES09/index2.html [accessed 26 June 2009]

8 **Flum DR**, Cheadle A, Prela C, Dellinger EP, Chan L. Bile duct injury during cholecystectomy and survival in medicare beneficiaries. *JAMA* 2003; **290**: 2168-2173 [PMID: 14570952 DOI: 10.1001/jama.290.16.2168]

9 **Way LW**, Stewart L, Gantert W, Liu K, Lee CM, Whang K, Hunter JG. Causes and prevention of laparoscopic bile duct injuries: analysis of 252 cases from a human factors and cognitive psychology perspective. *Ann Surg* 2003; **237**: 460-469 [PMID: 12677139 DOI: 10.1097/01.SLA.0000060680.92690.E9]

10 **Connor S**, Garden OJ. Bile duct injury in the era of laparoscopic cholecystectomy. *Br J Surg* 2006; **93**: 158-168 [PMID: 16432812 DOI: 10.1002/bjs.5266]

11 **Gregg RO**. The case for selective cholangiography. *Am J Surg* 1988; **155**: 540-545 [PMID: 3354777 DOI: 10.1016/S0002-9610(88)80406-9]

12 **Fiore NF**, Ledniczky G, Wiebke EA, Broadie TA, Pruitt AL, Goulet RJ, Grosfeld JL, Canal DF. An analysis of perioperative cholangiography in one thousand laparoscopic cholecystectomies. *Surgery* 1997; **122**: 817-21; discussion 821-3 [PMID: 9347861 DOI: 10.1016/S0039-6060(97)90092-1]

13 **Pesce A**, Portale TR, Minutolo V, Scilletta R, Li Destri G, Puleo S. Bile duct injury during laparoscopic cholecystectomy without intraoperative cholangiography: a retrospective study on 1,100 selected patients. *Dig Surg* 2012; **29**: 310-314 [PMID: 22986956 DOI: 10.1159/000341660]

14 **Ishizawa T**, Bandai Y, Ijichi M, Kaneko J, Hasegawa K, Kokudo N. Fluorescent cholangiography illuminating the biliary tree during laparoscopic cholecystectomy. *Br J Surg* 2010; **97**: 1369-1377 [PMID: 20623766 DOI: 10.1002/bjs.7125]

15 **Scroggie DL**, Jones C. Fluorescent imaging of the biliary tract during laparoscopic cholecystectomy. *Ann Surg Innov Res* 2014; **8**: 5 [PMID: 25317203 DOI: 10.1186/s13022-014-0005-7]

16 **Dip F**, Roy M, Lo Menzo E, Simpfendorfer C, Szomstein S, Rosenthal RJ. Routine use of fluorescent incisionless cholangiography as a new imaging modality during laparoscopic cholecystectomy. *Surg Endosc* 2015; **29**: 1621-1626 [PMID: 25277476 DOI: 10.1007/s00464-014-3853-7]

17 **Larsen SS**, Schulze S, Bisgaard T. Non-radiographic intraoperative fluorescent cholangiography is feasible. *Dan Med J* 2014; **61**: A4891 [PMID: 25162446]

18 **Osayi SN**, Wendling MR, Drosdeck JM, Chaudhry UI, Perry KA, Noria SF, Mikami DJ, Needleman BJ, Muscarella P, Abdel-Rasoul M, Renton DB, Melvin WS, Hazey JW, Narula VK. Near-infrared fluorescent cholangiography facilitates identification of biliary anatomy during laparoscopic cholecystectomy. *Surg Endosc* 2015; **29**: 368-375 [PMID: 24986018 DOI: 10.1007/s00464-014-3677-5]

19 **Daskalaki D**, Fernandes E, Wang X, Bianco FM, Elli EF, Ayloo S, Masrur M, Milone L, Giulianotti PC. Indocyanine green (ICG) fluorescent cholangiography during robotic cholecystectomy: results of 184 consecutive cases in a single institution. *Surg Innov* 2014; **21**: 615-621 [PMID: 24616013 DOI: 10.1177/1553350614524839]

20 **Dip FD**, Asbun D, Rosales-Velderrain A, Lo Menzo E, Simpfendorfer CH, Szomstein S, Rosenthal RJ. Cost analysis and effectiveness comparing the routine use of intraoperative fluorescent cholangiography with fluoroscopic cholangiogram in patients undergoing laparoscopic cholecystectomy. *Surg Endosc* 2014; **28**: 1838-1843 [PMID: 24414461 DOI: 10.1007/s00464-013-3394-5]

21 **Verbeek FP**, Schaafsma BE, Tummers QR, van der Vorst JR, van der Made WJ, Baeten CI, Bonsing BA, Frangioni JV, van de Velde CJ, Vahrmeijer AL, Swijnenburg RJ. Optimization of near-infrared fluorescence cholangiography for open and laparoscopic surgery. *Surg Endosc* 2014; **28**: 1076-1082 [PMID: 24232054 DOI: 10.1007/s00464-013-3305-9]

22 **Buchs NC**, Pugin F, Azagury DE, Jung M, Volonte F, Hagen ME, Morel P. Real-time near-infrared fluorescent cholangiography could shorten operative time during robotic single-site cholecystectomy. *Surg Endosc* 2013; **27**: 3897-3901 [PMID: 23670747 DOI: 10.1007/s00464-013-3005-5]

23 **Spinoglio G**, Priora F, Bianchi PP, Lucido FS, Licciardello A, Maglione V, Grosso F, Quarati R, Ravazzoni F, Lenti LM. Real-time near-infrared (NIR) fluorescent cholangiography in single-site robotic cholecystectomy (SSRC): a single-institutional prospective study. *Surg Endosc* 2013; **27**: 2156-2162 [PMID: 23271272 DOI: 10.1007/s00464-012-2733-2]

24 **Schols RM**, Bouvy ND, Masclee AA, van Dam RM, Dejong CH, Stassen LP. Fluorescence 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]

25 **Kaneko J**, Ishizawa T, Masuda K, Kawaguchi Y, Aoki T, Sakamoto Y, Hasegawa K, Sugawara Y, Kokudo N. Indocyanine green reinjection technique for use in fluorescent angiography concomitant with cholangiography during laparoscopic cholecystectomy. *Surg Laparosc Endosc Percutan Tech* 2012; **22**: 341-344 [PMID: 22874684 DOI: 10.1097/SLE.0b013e3182570240]

26 **Sherwinter DA**. Identification of anomolous biliary anatomy using near-infrared cholangiography. *J Gastrointest Surg* 2012; **16**: 1814-1815 [PMID: 22752550 DOI: 10.1007/s11605-012-1945-z]
27 **Buchs NC**, Hagen ME, Pugin F, Volonte F, Bucher P, Schiffer E, Morel P. Intra-operative fluorescent cholangiography using indocyanin green during robotic single site cholecystectomy. *Int J Med Robot* 2012; **8**: 436-440 [PMID: 22648637 DOI: 10.1002/rcs.1437]
28 **Ishizawa T**, Kaneko J, Inoue Y, Takemura N, Seyama Y, Aoki T, Beck Y, Sugawara Y, Hasegawa K, Harada N, Ijichi M, Kusaka K, Shibasaki M, Bandai Y, Kokudo N. Application of fluorescent cholangiography to single-incision laparoscopic cholecystectomy. *Surg Endosc* 2011; **25**: 2631-2636 [PMID: 21424202 DOI: 10.1007/s00464-011-1616-2]
29 **Ishizawa T**, Bandai Y, Hasegawa K, Kokudo N. Fluorescent cholangiography during laparoscopic cholecystectomy: indocyanine green or new fluorescent agents? *World J Surg* 2010; **34**: 2505-2506 [PMID: 20563724 DOI: 10.1007/s00268-010-0676-0]
30 **Aoki T**, Murakami M, Yasuda D, Shimizu Y, Kusano T, Matsuda 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: 19844652 DOI: 10.1007/s00534-009-0197-0]
31 **Pertsemlidis 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]
32 **Ishizawa T**, Bandai Y, Kokudo N. Fluorescent cholangiography using indocyanine green for laparoscopic cholecystectomy: an initial experience. *Arch Surg* 2009; **144**: 381-382 [PMID: 19380655 DOI: 10.1001/archsurg.2009.9]
33 **Ishizawa T**, Tamura S, Masuda K, Aoki T, Hasegawa K, Imamura H, Beck Y, Kokudo N. Intraoperative fluorescent cholangiography using indocyanine green: a biliary road map for safe surgery. *J Am Coll Surg* 2009; **208**: e1-e4 [PMID: 19228492 DOI: 10.1016/j.jamcollsurg.2008.09.024]

34 **Benya R**, Quintana J, Brundage B. Adverse reactions to indocyanine green: a case report and a review of the literature. *Cathet Cardiovasc Diagn* 1989; **17**: 231-233 [PMID: 2670244 DOI: 10.1002/ccd.1810170410]

35 **Tagaya N**, Shimoda M, Kato M, Nakagawa A, Abe A, Iwasaki Y, Oishi H, Shirotani N, Kubota K. Intraoperative exploration of biliary anatomy using fluorescence imaging of indocyanine green in experimental and clinical cholecystectomies. *J Hepatobiliary Pancreat Sci* 2010; **17**: 595-600 [PMID: 19806299 DOI: 10.1007/s00534-009-0195-2]

Footnotes

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

PRISMA 2009 Checklist statement:

Figure Legends

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

Ref.	Technique	*n*	CD	CHD	CD–CHD junction	CBD	CA
Larsen*et al*[17]	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*[16]	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*[20]	LC	43	42 (97.6)	25 (58.1)	-	34 (79.1)	-
Verbeek *et al*[21]	LC	14	14 (100)	-	-	-	-
Buchs *et al*[22]	SIRC	23	23 (100)	-	-	-	-
Spinoglio *et al*[23]	SIRC	45	42 (93.0)	40 (80.0)	40 (80.0)	41 (91.0)	-
Schols *et al*[24]	LC	15	15 (100)	-	-	15 (100)	-
Buchs *et al*[27]	SIRC	12	11 (91.7)	4 (33.3)	3 (25.0)	6 (50.0)	-
Kaneko *et al*[25]	LC	28	26 (92.9)	27 (96.4)	-	-	25 (89)
Ishizawa *et al*[28]	SILC	7	5 (71.4)	7 (100)	7 (100)	-	4 (57.1)
Aoki *et al*[30]	LC	14	10 (71.4)	-	-	10 (71.4)	-

Ref.	Technique	*n*	CD	CHD	CD–CHD junction	CBD	CA
Ishizawa *et al*[32]	LC	52	52 (100)	50 (96.2)	50 (96.2)	-	-
Ishizawa *et al*[32]	LC	1	1 (100)	1 (100)	1 (100)	-	-
Weighted average, % (95% CI)			96.2 (94.7–97.7)	78.1 (74.8–81.4)	72.0 (69.0–75.0)	86.0 (83.3–88.8)	69.4 (61.8–77.1)

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 roboticcholecystectomy.

Table 2 Identification of biliary structures before and after Calot's dissection

Vascular structure	Ishizawa *et al*[14]		Osayi *et al*[18]		Spinoglio *et al*[23]		Buchs *et al.*[22]		Weighted average, % (95% CI)
	n/total	%	*n*/total	%	*n*/total	%	*n*/total	%	
Before dissection of Calot's triangle									
CD	52/52	100	46/82	56.1	42/45	93.3	11/12	91.7	79.1 (74.0–84.1)
CHD	50/52	96.1	29/82	35.4	40/45	88.8	4/12	33.3	64.4 (59.0–69.8)
CBD	-	-	31/82	37.8	41/45	91.1	6/12	50.0	56.1 (48.9–63.3)
CD–CHD junction	50/52	96.1	20/82	24.4	40/45	88.8	3/12	25.0	59.1 (54.1–64.1)
After dissection of Calot's triangle									
CD	52/52	100	78/82	95.1	44/45	97.7	12/12	100	97.4 (94.9–99.8)
CHD	52/52	100	57/82	69.5	44/45	97.7	8/12	66.6	84.3 (79.6–89.0)
CBD	-	-	63/82	76.8	44/45	97.7	10/12	83.3	84.1 (78.3–90.0)
CD–CHD junction	52/52	100	63/82	76.8	44/45	97.7	7/12	58.3	86.9 (82.5–91.3)

CD: Cystic duct; CHD: Common hepatic duct; CBD: Common biliary duct.

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*[22]		Weighted average, % (95% CI)
	n/total	%	*n*/total	%	*n*/total	%	
BMI > 30 kg/m^2							
CD	99/102	97.0	36/39	92.3	2/2	100	95.8 (92.5–99.0)
CHD	96/102	94.1	24/39	61.5	0/2	0	83.9 (80.0–87.8)
CBD	97/102	95.0	28/39	71.8	1/2	50.0	88.0 (83.1–93.0)
CD–CHD junction	84/102	82.3	26/39	66.6	0/2	0	76.9 (70.2–83.5)
BMI < 30 kg/m^2							
CD	81/82	98.8	42/43	97.7	9/10	90.0	97.1 (94.6–99.5)
CHD	77/82	93.9	33/43	76.7	4/10	40.0	84.4 (78.8–90.0)
CBD	80/82	97.5	35/43	81.4	5/10	50.0	88.9 (84.0–93.7)
CD–CHD junction	70/82	85.3	37/43	86.0	3/10	30.0	81.4 (75.3–87.5)

BMI: Body mass index; CBD: Common biliary 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*[20]	
	***n*/ total**	**%**	***n*/total**	**%**
CD	22/24	91.6	-	94.5
CHD	19/24	79.1	-	57.0
CBD	19/24	79.1	-	72.0
CD–CHD junction	18/24	75.0	-	-

CBD: Common biliary duct; CD: Cystic duct; CHD: Common hepatic duct.