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Use of fluorescence imaging and indocyanine green during laparoscopic cholecystectomy: Results of an international Delphi survey

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A R T I C L E I N F O

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A B S T R A C T

Background: Published empirical data have increasingly suggested that using near-infrared fluorescence cholangiography during laparoscopic cholecystectomy markedly increases biliary anatomy visualization. The technology is rapidly evolving, and different equipment and doses may be used. We aimed to identify areas of consensus and nonconsensus in the use of incisionless near-infrared fluorescent cholangiography during laparoscopic cholecystectomy.

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Methods: A 2-round Delphi survey was conducted among 28 international experts in minimally invasive surgery and near-infrared fluorescent cholangiography in 2020, during which respondents voted on 62 statements on patient preparation and contraindications ($n = 12$); on indocyanine green administration ($n = 14$); on potential advantages and uses of near-infrared fluorescent cholangiography ($n = 18$); comparing near-infrared fluorescent cholangiography with intraoperative x-ray cholangiography ($n = 7$); and on potential disadvantages of and required training for near-infrared fluorescent cholangiography ($n = 11$).
Results: Expert consensus strongly supports near-infrared fluorescent cholangiography superiority over white light for the visualization of biliary structures and reduction of laparoscopic cholecystectomy risks. It also offers other advantages like enhancing anatomic visualization in obese patients and those with moderate to severe inflammation. Regarding indocyanine green administration, consensus was reached that dosing should be on a milligrams/kilogram basis, rather than as an absolute dose, and that doses >0.05 mg/kg are necessary. Although there is no consensus on the optimum preoperative timing of indocyanine green injections, the majority of participants consider it important to administer indocyanine green at least 45 minutes before the procedure to decrease the light intensity of the liver.
Conclusion: Near-infrared fluorescent cholangiography experts strongly agree on its effectiveness and safety during laparoscopic cholecystectomy and that it should be used routinely, but further research is necessary to establish optimum timing and doses for indocyanine green.

Introduction

Patients undergoing cholecystectomy are at risk of potentially catastrophic biliary duct injury (BDI) for various reasons, including anatomic variations in the extrahepatic biliary tree, inadequate visualization of extrahepatic structures, and surgeon inexperience.[1,2] The introduction of laparoscopic cholecystectomy (LC) 30 years ago yielded several advantages for patients, but reduced BDI incidence was not among them. In fact, BDI incidence increased,[3,4] with the absence of tactile sensation and visual misperceptions secondary to the new optoelectronic instrumentation commonly implicated as responsible.[2,5,6] Irrespective of efforts to develop safer laparoscopic techniques for cholecystectomy and cholangiography and increased surgeon awareness, 30 years after LCs first were introduced, BDI incidence remains unacceptably high.[7–10]

Indocyanine green (ICG) is a fluorophore that responds to near-infrared irradiation, absorbing light between the wavelengths of 790 and 805 nm and re-emitting it with an excitation wavelength of 835 nm.[11] Since the initial use of ICG fluorescence imaging almost 50 years ago via the introduction of applied ophthalmic angiography,[12] its use has expanded exponentially[13] to include the identification of tumors and sentinel lymph nodes involving the breast,[14–16] lungs,[17,18] liver,[19,20] colon,[21,22] stomach,[21–23] and pelvis[24–28]; the assessment of tissue perfusion in viscera[19,22,29–31] and during plastic surgery[32,33]; identifying anastomotic leaks[34–36]; and assessing parathyroid gland vitality during thyroid and parathyroid resections.[37,38] It was approximately 2 decades ago that intraoperative fluorescent imaging made its first foray into endoscopic surgery on the liver and biliary tree.[39] In 2020, the superior effectiveness of ICG fluorescence over white light imaging was documented in a randomized controlled trial (RCT), in which the former was found to dramatically enhance the visualization of extrahepatic biliary structures, more than doubling and tripling their detection rate.[40] Nonetheless, variability continues to exist in the way ICG is administered during fluorescence-guided surgery, particularly pertaining to its dose and timing of administration, as well as in numerous other technical aspects of fluorescence imaging. Questions also persist regarding whether patients need to sign specific consent forms when near-infrared fluorescent cholangiography (NIFC) or ICG is used, if and when its use should be considered contraindicated, and other issues not addressed in clinical trials.

We are currently conducting a series of surveys to assess current practices in the use of fluorescence imaging across a broad range of indications and to identify areas of both consensus and nonconsensus among surgeons who are well-recognized experts in the field of fluorescence-guided surgery. For these purposes, we are employing a modified Delphi survey approach to permit anonymous voting and, thereby, reduce voter bias potentially caused by peer pressure. The present article describes the results of our survey among surgeons using ICG fluorescence imaging during LC, a technique called NIFC.

Methods

Expert recruitment and data collection

A Delphi survey was conducted in the summer of 2020, adhering to published guidelines.[41] The Delphi technique has been gaining increasing credence as a means to achieve consensus and identify areas of nonconsensus among experts across a wide variety of health- and non–health-related fields.[41]

Over the summer of 2019, e-mails were sent to members of the International Society for Fluorescence Guided Surgery (ISFGS), asking them to provide a list of questions they consider important relating to ICG use during procedures within their surgical field. These questions were screened and used to generate a series of Delphi surveys by experts within each specific surgical field. For the survey on LCs, the final statement items were selected by 2 investigators (F.D. and R.J.R.) and edited for clarity by a PhD-level expert in survey development and with further expertise in Delphi survey orchestration (K.P.W.). The final survey asked 4 questions on the nature of each expert's general surgical practice, followed by 62 consensus statements on which survey participants were asked to vote, divided into 5 modules: (1) patient preparation and contraindications ($n = 12$); (2) ICG dosing and administration ($n = 14$); (3) potential advantages and uses of NIFC ($n = 18$); (4) comparing NIFC with fluoroscopic intraoperative cholangiography (IOC) ($n = 7$); and (5) potential disadvantages of and required training for NIFC use ($n = 11$). Among these 62 statements, 48 had the binary response options of agree versus disagree, whereas 14 had multiple response options (eg, increases, decreases, and no impact).

During survey design, several approaches were employed to reduce the risk of acquiescence bias: the potential for the survey instrument itself to influence responses through the wording and/or order of its statements and/or response options. First, among statements that might be perceived as assessing the value of or indications/contraindications for NIFC, roughly an equal number were worded as unfavorably (eg, "NIFC should not be used in patients with known gallstones") as favorably (eg, "Allergic reactions to ICG are considered extremely rare"). Second, numerous nonjudgmental statements were included. Third, the order of response options was varied, sometimes listing the most fluorescence imaging–agreeable option first, sometimes in the middle, and sometimes last.

The list of experts used to enlist survey participants was generated using the following eligibility criteria: (1) authorship for a published clinical study evaluating the use of NIFC, or (2) ≥10 years in surgical practice and 5 years using NIFC during LC; also, every participant also had to (3) be acknowledged as an international expert by current members of the ISFGS Advisory Board, (4) be fluent in written English, (5) express willingness to participate in the survey, and (6) also express willingness to review and approve the paper before submission for publication. This ultimately resulted in a list of 33 international experts across 5 continents, among whom 28 ultimately participated in the survey. The majority of these experts had no affiliation with ISFGS.

Once the list of willing experts was generated, the first of ≤3 e-mails was sent by the survey's lead authors (F.D. and R.J..R) to all of the names on the list of experts, asking them again to participate in this survey examining the use of NIFC during LC and providing a link to the survey using the online application SurveyMonkey. On the online page provided, voting was conducted electronically, with follow-up e-mails sent to all nonrespondents once weekly for 3 weeks, followed by a telephone call from R.J.R. to any who had not yet responded to the survey. Round 1 was considered completed within 1 week of the above-noted telephone calls, and all of the collected round 1 data were analyzed to identify the degree of consensus reached with each of the 62 statements. Based on published guidelines,[41] an a priori decision had been made to consider 70% agreement between voters as evidence of consensus. Only statements for which either consensus was not reached or exactly 70% consensus was reached (to confirm borderline consensus) were included in the round 2 survey, for which all 33 experts again were sent an e-mail and link to a SurveyMonkey survey page, adhering to the same e-mail, telephone, and data collection termination protocol employed for round 1. Along with the statements for which no round 1 consensus had been achieved, round 2 participants were also provided, for each item, the percentage of participants who had selected each response option in round 1 (eg, percent consensus), again following published Delphi survey guidelines.[41]

Data analysis

Because our purpose was to report areas and degrees of consensus, and all of the responses were managed to maintain responders' anonymity, inferential analysis was deemed neither appropriate nor feasible. The percentage agreement—defined as agreement between responders rather than agreement with any given statement—was calculated as the number of voters selecting the most commonly selected response divided by the total number of experts voting on that particular statement, multiplied by 100%, with ≥70% agreement between voters considered consensus reached and <70% agreement considered nonconsensus. The percentage participation also was calculated per item as the number of experts voting on each item divided by the total number of experts participating in that round (round 1 or 2), again multiplied by 100%, with 80% participation considered a valid response. For quality control, all of the data were analyzed using SurveyMonkey's intrinsic data analysis tool and again in Windows Excel, version 16 (Microsoft, Corp, Redmond, WA)

Table I
Demographics and practice characteristics of the expert panel

Practice characteristic	Number	Percentage
Region of practice ($N = 28$)		
Asia-Pacific	2	7.1
Europe	12	42.9
North America	11	39.3
Central and South America	3	10.7
Nature of practice ($N = 28$)		
Primarily university based	14	50.0
Some university affiliation	13	46.4
Nonacademic	1	3.6
Years performing laparoscopic cholecystectomies ($N = 27$)		
<10 y	3	11.1
10–20 y	10	37.0
>20 y	14	51.9
Years using fluorescent cholangiography with indocyanine green ($N = 28$)		
<5 y	9	32.1
5–10 y	15	53.6
> 10 y	4	14.3

20 experts voted in the first round, whereas 23 voted in the second round. Of the 20 who voted in the first round, 15 voted again in the second round. Eight experts voted only in the second round.
The total number of experts contacted and invited to participate was 33, meaning that the overall rate of participation was 84.8% (60.6% in the first round and 69.7% in the second round).

Results

Expert characteristics

Of the 33 experts who initially agreed to participate in this survey, 28 (88.4%) participated—20 in round 1 (60.6% of the initially invited 33) and 23 in round 2 (69.7%); 15 experts participated in both rounds. Table I summarizes the practice characteristics of the 28 who participated in either 1 or both rounds of the survey.

Consensus results—overview

The lowest response rate among participants for any item in either round was 95%; consequently, all of the responses were considered valid. Among the 62 statements for which consensus was sought, 23 were worded in a way deemed favorable and 17 unfavorable to fluorescent imaging, whereas 22 were considered nonjudgmental (Table II). Consensus was reached on 57 statements—42 in round 1 and 15 in round 2—at a mean 87.4% level. The range of agreement between experts was from 56.5% to 100%, with 100% consensus reached on 13 items (21%), 90% to 99% on 21 (34%), 80% to 89% on 15 (24%), and 74% to 79% on 8 (13%); the minimum level of consensus achieved, among statements in which consensus ultimately was reached, was 73.9%. In round 1, borderline consensus (70%) was achieved on 5 statements, all of which were re-presented in the second round (per study protocol), during which a greater percentage of consensus was achieved for all 5 (in Tables III, IV, and VI, indicated with an asterisk). Among the 44 statements for which experts were asked to agree or disagree, agreement with the statement was the consensus opinion for 27 and disagreement for 17 (Table II).

Consensus results—specifics

Tables III to VII summarize the results for modules 1 through 5 of the survey. Across the 12 statements pertaining to preoperative patient preparation and contraindications against NIFC (module 1), consensus was reached on 10, ranging from 75% to 100%, with >70% consensus reached for 3 in round 2 (Table III). The 2 statements that

Table II
Overall summary of results

	Number	Percentage
Total number of statements	62	
Consensus reached	57	91.9
No consensus reached	5	8.1
Consensus reached in first round	42	67.7
Consensus reached in second round	15	24.2
100% consensus reached	13	21.0
90%–99% consensus reached	21	33.9
80%–89% consensus reached	15	24.2
70%–79% consensus reached	8	12.9
Statements agreed with (total)	27	43.5
Statements disagreed with (total)	17	27.4
Statements agreed with (consensus)	25	40.3
Statements disagreed with (consensus)	16	25.8
Statements worded favorably to FC/ICG	23	37.1
Statements worded unfavorably to FC/ICG	17	27.4
Nonjudgmental statements	22	35.5
Average consensus	87.4%	
Minimum/maximum consensus	56.5/100%	
Minimum when consensus reached	73.9%	

Data on the number and percentage of statements worded favorably, unfavorably, and nonjudgmentally refer to the study's overall risk of bias and validity.
FC, fluorescent cholangiography; *ICG*, indocyanine green.

achieved unanimous consensus were that allergic reactions to ICG are rare and that NIFC can be used in patients with gallstones. The 2 statements for which no consensus was achievable both pertained to whether known or suspected allergy to either iodine or shellfish was either a relative or absolute contraindication to using ICG.

With respect to ICG administration (module 2, Table IV), >70% consensus was observed for 12 of 14 statements, the 2 exceptions relating to the use of intrabiliary ICG injection when biliary structures are not visualized after intravenous (IV) ICG administration (with 61% of respondents favoring such use) and to the optimum timing of IV ICG administration before NIFC, opinions roughly evenly split between injecting from 30 to 60 minutes and >60 minutes beforehand (43.5% and 56.5%, respectively). Where consensus was reached, it generally was strong: ≥90% for 10 of 12 statements, including 100% consensus on 3. Interestingly, given the relative lack of consensus regarding optimum timing, other than that it should be administered at least 30 minutes before the procedure, 100% agreed that the timing of ICG administration for NIFC is very important. Complete (100%) consensus was also attained, with disagreement that biliary stones are an indication for the intrabiliary injection of ICG but agreement that the biliary artery becomes visible within seconds to minutes of IV ICG administration.

At least 75% consensus was observed for all 18 statements on potential advantages and uses of NIFC (module 3, Table V). For 16 of these statements, the consensus was that NIFC is advantageous or of value. Consensus was reached for only 2 statements that NIFC is not of particular value, pertaining to the visualization of gallstones and decreasing the risk of major hemorrhage. Ninety percent of the experts agreed that NIFC should be used routinely, rather than selectively, for LCs; and 75% felt it was always necessary.

Comparing NIFC with fluoroscopic IOC (module 4, Table VI), consensus was reached that NIFC is faster, safer, and less expensive and that it decreases the risk of LC overall and BDI specifically. Conversely, 95% and 90% consensus levels also were reached that NIFC is no better than IOC at visualizing gallstones and that it does not completely replace IOC.

Among potential disadvantages of NIFC (module 5, Table VII), there was consensus agreement that inadequate equipment availability and background fluorescence are major limitations but also that inadequate empirical evidence supporting NIFC use and regulatory issues are not so. Complete (100%) consensus was reached that the use of NIFC (specifically using ICG) is likely to increase both in clinical practice and research over the next decade and that NIFC is useful for training surgical residents. There also was strong consensus (87% and 85%) that not just surgery residents, but also residents in nonsurgical fields, should learn about fluorescence imaging and that such exposure should begin in medical school. The only statement in this module for which >70% consensus was not reached pertained to the number of NIFC cases required to overcome the learning curve, with 56.5% selecting 11 to 25 cases but 43.5% selecting 10 or less; no one believed >25 cases were required to become proficient in NIFC use.

Discussion

Considerable evidence has already been published documenting the effectiveness of fluorescence imaging and ICG across a broad range of fields and procedures, including ophthalmology,[12] virtually all branches of oncological surgery,[13] plastic surgery,[32,33] nononcological gastrointestinal[21,29,30,42] and endocrine surgery,[37,38] lymphatic surgery,[43,44] and others.

Pertaining to LCs and the use of NIFC, the most convincing supportive evidence stems from a recently published, 5-nation RCT in which LC was performed either using NIFC as an adjunct to visualization under white light ($n = 321$) or employing white light alone.[40] In this study, the detection rates for the 4 extrahepatobiliary ducts—cystic, right hepatic, common hepatic, and common bile[45]—were 130% to 260% higher with NIFC than white light, as they also were for the cystic–common bile duct junction, cystic–gallbladder junction, and accessory ducts before dissection. Similar superiority of NIFC over white light was observed after dissection and in the settings of patient obesity and moderate to severe inflammation. Only 2 procedures resulted in a BDI, both in the white light–only group; and, of the 5 conversions required across the 639 patients, 4 occurred in white light–only patients (2 for BDI and 2 for inadequate biliary visualization), whereas the only conversion that occurred in the NIFC group was for bleeding. Finally, among the 37 surgeons who participated in the surgery, 83% and 82% considered NIFC safer and felt more confident using NIFC than white light alone, respectively, whereas only 1 considered NIFC less safe and 2 felt less confident using it.[40] To date, the only other published RCT studying NIFC was a noninferiority study involving 120 patients ($n = 60$ per group) comparing NIFC with IOC,[46] in which detection rates for the critical junction between the cystic, common hepatic, and common bile ducts were almost identical. However, although NIFC was completed in all 60 patients in the study's NIFC arm, IOC was deemed infeasible in 9 patients in the IOC arm. The NIFC also took less than half the time to complete. A meta-analysis also recently has been published comparing the use of NIFC ($n = 1603$ patients) with white light alone ($n = 5070$) in rates of BDI and conversion to open surgery, in which the rates were only one fourth and one seventeenth as high, respectively, in patients undergoing NIFC.[47]

One area of nonconsensus deemed very important among experts in the current survey was the timing of IV ICG administration. Three published studies have attempted to establish the optimum time for ICG injection: in Japan,[48] China,[49] and the Netherlands.[50] For all 3 studies, the primary outcome was the ratio of fluorescence in bile ducts versus background tissues (eg, liver). The results of 1 of these studies suggested that ICG should be administered >3 to 5 hours before surgery, depending on the ICG dose administered (5 vs 10 mg),[50] whereas the other 2 suggested that 8 to 15 hours preoperatively is best.[51,49] This said, in their review of 27 trials, Boogerd et al[50] found that most studies employed 2.5 mg

Table III
Module 1—statements regarding patient preparation and contraindications

Statement	Votes (no.)	Response	Rounds (no.)	Consensus (%)
Consensus reached				
Allergic reactions to ICG are extremely rare.	20	Agree	1	100
FC with ICG should not be used in patients with known gallstones.	20	Disagree	1	100
All patients should be asked about possible allergies to iodine, shellfish or ICG before having ICG administered.	20	Agree	1	95.0
Inability to provide informed written consent is a relative contraindication to using FC with ICG.*	23	Disagree	2	91.3
Before undergoing FC with ICG, patients should be informed that its use is still experimental.	20	Disagree	1	90.0
Before undergoing FC with ICG, patients must provide informed written consent specific to the use of FC with ICG.	23	Disagree	2	82.6
Inability to provide informed written consent is an absolute contraindication to using FC with ICG.	20	Disagree	1	80.0
Pregnancy is an absolute contraindication to FC with ICG.	20	Disagree	1	75.0
Pregnancy is a relative contraindication to FC with ICG.	20	Disagree	1	75.0
Before undergoing FC with ICG, patients should be provided with written information specifically addressing the use of FC with ICG.*	23	Disagree	2	73.9
No consensus reached				
Known or suspected allergy to iodine or shellfish is an absolute contraindication to FC with ICG.	23	Agree	2	60.9
Known or suspected allergy to iodine or shellfish is a relative contraindication to FC with ICG.	23	Disagree	2	56.5

FC, fluorescent cholangiography; *ICG*, indocyanine green.
* Borderline (70%) consensus in round 1.

administered within 1 hour of imaging, whereas imaging from 3 to 24 hours post ICG administration was never studied. In the RCT by Dip et al,[40] ICG was injected roughly 45 minutes before surgery, whereas the timing of ICG administration was not mentioned for the other NIFC RCT.[46] What is notable for every study mentioned above is that, despite variable timing, ICG always was injected in advance of the surgery, contrary to the ICG typically given just seconds to at most a few minutes before anastomosis and tissue perfusion assessments in gastrointestinal and plastic surgery.

From our survey of 28 international experts in NIFC, it is clear that strong consensus exists on most issues relating to NIFC indications, contraindications, advantages, and disadvantages/limitations and, regarding the increasing role that NIFC is likely to play, going forward, in both clinical practice and research. Consensus was reached that, relative to white light, NIFC appreciably enhances the visualization of biliary structures, including aberrant biliary anatomy; visualization even with moderate to severe inflammation, including patients with acute cholecystitis; and biliary tract visualization, even in patients with gallstones or obesity. It also reduces overall surgical risk and the risks of both BDI and conversions to open surgery.

Consensus was that it has several advantages over IOC, but also that it cannot entirely replace it and is not better at visualizing gallstones. Pertaining to how to administer ICG, consensus was that it should be dosed on a milligrams/kilogram basis, rather than as an absolute dose, and that doses >0.05 mg/kg are necessary. However, no consensus was reached on the optimum timing of ICG administration—other than that it should be injected ≥30 minutes before the procedure—which reflects the wide discrepancies in current literature.[40,49–51] We also noted that differences in the fluorescence camera used might have an impact on when and how to administer ICG, an issue our survey did not address.

As detailed extensively in the introductory article for this special issue and again in the final summary article, any opinion study has limitations. Perhaps the greatest criticism given of Delphi studies is that bias favoring a given approach is inevitable among those who have become experts using it: why would anyone decide to become an expert using an approach they do not already value? Conversely, asking such experts to comment on a given therapeutic or diagnostic approach has the advantage that, besides having extensive clinical experience, they also are invariably familiar with the published literature, many having actively contributed to it, and,

Table IV
Module 2—statements regarding indocyanine green dosing and administration

Statement	Votes (no.)	Response	Rounds (no.)	Consensus (%)
Consensus reached				
For FC with ICG, the timing of ICG administration (how long before the surgery) is very important.	20	Agree	1	100
Biliary stones are an indication for the intrabiliary injection of ICG.	23	Disagree	2	100
After the IV injection of ICG, the biliary artery usually becomes visible within seconds to, at most, minutes.	20	Agree	1	100
For FC with ICG, the concentration of ICG administered is very important.*	23	Agree	2	95.7
The dose of ICG to administer for FC should be determined on a mg per kg basis or as an absolute dose.	23	Milligrams/ kilogram	2	95.7
Cystic duct obstruction is an indication for the intrabiliary injection of ICG.	22	Disagree	2	95.5
Intrabiliary injection of ICG can be used for FC.	20	Agree	1	95.0
IV injection of ICG can be used to visualize the biliary artery.	20	Agree	1	95.0
A second IV dose of ICG is usually required to visualize the biliary artery intraoperatively.	20	Agree	1	95.0
The optimum dose of ICG to administer before a laparoscopic cholecystectomy is…	20	>0.05 mg/kg	1	90.0
For FC with ICG, the dose of ICG administered is very important	20	Agree	1	85.0
Research is necessary to determine the optimum dose and concentration of ICG and timing of ICG administration.	20	Agree	1	85.0
No consensus reached				
Failure to observe biliary structures after IV injection of ICG is an indication for the intrabiliary injection of ICG.	23	Agree	2	60.9
The optimum timing of ICG administration before a laparoscopic cholecystectomy is…	23	>60 min	2	56.5

FC, fluorescent cholangiography; *ICG*, indocyanine green; *IV*, intravenous.
* Borderline (70%) consensus in round 1.

Table V
Module 3—statements regarding potential advantages/uses of fluorescent cholangiography with indocyanine green

Statement	Votes (no.)	Response	Rounds (no.)	Consensus (%)
Consensus reached				
FC with ICG is useful for LC in patients with acute/severe cholecystitis.	20	Agree	1	100
FC with ICG is useful for LC in patients with gallstones.	19	Agree	1	100
Enhanced visualization of aberrant EHB anatomy is an advantage of FC with ICG over WLO.	20	Agree	1	100
Enhanced visualization of accessory bile ducts is an advantage of FC with ICG over WLO.	20	Agree	1	100
FC with ICG increases the pre-dissection visualization of all extrahepatic biliary structures essential for LC to >75%.	23	Agree	2	95.7
FC with ICG significantly enhances pre-dissection visualization of extrahepatic biliary structures relative to white light alone.	20	Agree	1	95.0
FC with ICG increases the pre-dissection visualization of all extrahepatic biliary structures essential for LC to >50%.	20	Agree	1	95.0
Relative to white light alone, FC with ICG increases, decreases, or has no impact on the risk of bile duct injury.	20	Decreases	1	95.0
Enhanced visualization of EHB structures in patients with moderate to severe inflammation is an advantage of FC with ICG over WLO.	20	Agree	1	95.0
For LCs, FC with ICG should be used routinely or selectively	20	Routinely	1	90.0
FC with ICG have a significantly impact on the way that LCs are performed.	20	Agree	1	90.0
Relative to white light alone, FC with ICG increases, decreases, or has no impact on the overall risk of LC.	20	Decreases	1	90.0
Relative to white light alone, FC with ICG increases the visualization of gallstones.	23	Disagree	2	87.0
Relative to white light alone, FC with ICG increases, decreases, or has no impact on the rate of conversion to open surgery.	20	Decreases	1	85.0
Enhanced visualization of EHB structures in obese patients is an advantage of FC with ICG over WLO.	20	Agree	1	85.0
Relative to white light alone, FC with ICG increases, decreases, or has no impact on the risk of major hemorrhage.	23	No impact	2	82.6
Relative to white light alone, FC with ICG increases, decreases, or has no impact on the overall time required to perform LC.	20	Decreases	1	75.0
FC with ICG is necessary for all LCs.	20	Agree	1	75.0

EHB, extrahepatic biliary; *FC*, fluorescent cholangiography; *ICG*, indocyanine green; *IV*, intravenous; *LC*, laparoscopic cholecystectomy; *WLO*, white light alone.

therefore, are likely best equipped to interpret it. Our cholecystectomy panel clearly perceived value in NIFC, reaching 75% consensus that it should be used during every LC procedure. However, this opinion is supported by the results of both a large multicenter RCT and a meta-analysis, the latter documenting markedly reduced rates of BDI and conversions to open surgery to one-fourth and one-seventeenth the rates observed without it.[47] Moreover, despite the obvious support of NIFC overall, there were statements unfavorable to this technology that the panel agreed with; for example, that it is not useful for visualizing gallstones and has no impact on the risk of hemorrhage. As well, experts for some of the other Delphi studies published in this special issue, selected by the same means as the experts selected for this survey, reached consensus disagreeing with the value of fluorescence imaging for certain purposes: for example, although our panel of colorectal surgery experts agreed that fluorescence imaging has value assessing anastomosis perfusion, they also were much less supportive of its use detecting sentinel lymph nodes in colorectal cancer patients, both conclusions supported by several published meta-analyses.[34,36,52−57] Similarly, whereas our gastric cancer surgery panel saw value in fluorescence imaging detecting sentinel lymph nodes, as found in a published RCT,[16] they still considered its use experimental, given uncertainty regarding its impact on the extent of surgical resections or patient survival.

We also attempted to address this potential bias by enlisting the participation of a broad spectrum of experts, in terms of geography, nature of practice, and years of experience, most of whom had no affiliation with ISFGS, and tried to minimize any influence the survey itself might have on responses by balancing statements favoring and not favoring NIFC and by altering the order of favorable versus nonfavorable response options. Notwithstanding these attempts, we emphasize the dire need for further research to validate the opinions expressed herein, in particular further RCTs, and are heartened that such studies are, indeed, already underway. In conclusion, expert consensus strongly supports the superiority of NIFC with ICG over white light for the visualization of biliary structures and reduction of risks for most LC indications. It offers other advantages as well, including being faster than IOC and enhancing anatomic visualization in obese patients and those with moderate to severe inflammation. This said, adding IOC to NIFC

Table VI
Module 4—statements comparing fluorescent cholangiography with indocyanine green versus intraoperative x-ray cholangiography

Statement	Votes (no.)	Response	Rounds (no.)	Consensus (%)
Consensus reached				
Relative to intraoperative x-ray cholangiography, FC with ICG is about as quick, faster, or slower to perform.	19	Faster	1	100
FC with ICG is better than intraoperative x-ray cholangiography at visualizing gallstones.	19	Disagree	1	94.7
FC with ICG completely replaces intraoperative x-ray cholangiography.	20	Disagree	1	90.0
Relative to intraoperative x-ray cholangiography, FC with ICG is less safe, safer, or about as safe.	19	Safer	1	89.5
Relative to intraoperative x-ray cholangiography, FC with ICG increases, decreases, or has no impact on the overall risk of LC.*	23	Decreases	2	87.0
Relative to intraoperative x-ray cholangiography, FC with ICG is about the same cost, less expensive, or more expensive.	20	Less expensive	1	85.0
Relative to intraoperative x-ray cholangiography, FC with ICG increases, decreases, or has no impact on the overall risk of BDI.*	23	Decreases	2	78.3

FC, fluorescent cholangiography; *ICG*, indocyanine green; *LC*, laparoscopic cholecystectomy;
* Borderline (70%) consensus in round 1.

Table VII
Module 5—statements regarding potential disadvantages and training

Statement	Votes (no.)	Response	Rounds (no.)	Consensus (%)
Consensus reached				
FC with ICG is useful for training surgical residents.	20	Agree	1	100
Over the next decade, the use of FC with ICG in surgical practice is likely to increase, decrease, or stay the same.	20	Increase	1	100
Over the next decade, the use of FC with ICG in research is likely to increase, decrease, or stay the same.	20	Increase	1	100
Equipment unavailability is a major limitation to performing FC with ICG.	20	Agree	1	90.0
Exposure of physician trainees to fluorescent imaging should begin during medical school or residency training.	23	Medical school	2	87.0
Not just surgery residents, but residents in other nonsurgical fields should learn about fluorescent imaging.	20	Agree	1	85.0
Inadequate empirical evidence supporting efficacy is a major limitation to performing FC with ICG.	20	Disagree	1	80.0
Background fluorescence is a significant disadvantage of using FC with ICG.	20	Agree	1	80.0
Visualization of the extrahepatic ducts (not the cystic duct) is a violation of the CVS technique and should not be pursued.	23	Disagree	2	78.3
Regulatory issues are a major limitation to performing FC with ICG.	23	Disagree	2	73.9
Consensus not reached				
The number of cases of FC with ICG that need to be completed to overcome the learning curve is approximately…	23	11–25 cases	2	56.5

CVS, critical view of safety; *FC*, fluorescent cholangiography; *ICG*, indocyanine green; *LC*, laparoscopic cholecystectomy.

could increase safety and decrease complications in select cases. Although further research is necessary to establish logistics like the optimum timing of ICG administration, NIFC should no longer be considered experimental.

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Conflict of interest/Disclosure

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