14 The Indocyanine Green Role in Acute Cholecystitis

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Objectives
This chapter aims to:

- Define difficult acute cholecystitis.
- Review the appropriate management of difficult acute cholecystitis.
- Review the outcomes following the adequate approach to difficult acute cholecystitis.

14.1 Introduction

Cholecystectomy continues to be among the most commonly performed surgeries in the United States (US) and developed countries. Currently, more than 90% of the cholecystectomies performed in the US are performed laparoscopically, and an open approach is no longer considered standard of care. LC is recognized as the therapeutic gold standard of benign gallbladder (GB) disease, and it has been associated with short hospital stay and fewer postoperative complications when compared to the open approach [1]. Current and ongoing advances in optical and surgical devices, improvement in surgical techniques, and the introduction of novel technologies have skewed this recommendation.

Acute cholecystitis is a common complication of gallstone disease, imposing a latent risk of developing surgical complications such as bleeding and bile duct injuries (BDI), if managed improperly [2]. The incidence of BDIs during LC ranges from 0.2% to 1.1% [3–5]. The implications of BDI following LC extend beyond the significant medical complications and encompass increased medical costs, litigation, and decrease in quality of life [6–8]. The first treatment guidelines for AC based on severity criteria were published in 2007 and provided a thorough understanding on how to adequately manage AC in accordance to clinical appearance.

Up until now, LC has been widely implemented as surgical therapy for AC. However, it is well known that patients undergoing LC for AC have twice the risk of sustaining a BDI when compared to patients without AC. Several techniques have been described to limit BDIs in this particular setting. Among these, the use of intraoperative cholangiography (IOC) has been shown to decrease severity of the BDI, but not necessarily their occurrence [9].

This chapter focuses on the surgical aspects of adequate management of AC through LC.

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14.2 Acute Cholecystitis

14.2.1 Severity of Acute Cholecystitis

The first treatment guidelines for AC of different levels of severity were published in 2007. Since then, there have been several updates and modifications. The 2018 Tokyo Guidelines (TG18) have indicated three levels of severity for AC. These levels are summarized in Table 14.1.

The recognition of the severity level of AC remains paramount for safe operative planning. Based on this severity stratification, the surgeon can objectively analyze the potential pitfalls and technical shortcomings of surgical intervention. All of these will undoubtedly have an impact on the ease of the surgery and patient outcomes. Prior to the introduction of the critical view of safety for the dissection of Calot's triangle and the evolution of visual optics in laparoscopic equipment, LC for AC was not considered the gold standard [10, 11].

The performing surgeon should be aware that an intra-abdominal image translated into even a high-resolution two-dimensional screen presents shortfalls based on the different haptic feedback and visual misperceptions. The improvement of optoelectronic instrumentation and increased surgical experience has decreased the learning curve for this and many other surgical procedures. Nonetheless, it is imperative to identify the risk factors associated with the levels of severity for AC. Similar to other laparoscopic procedures, the surgical difficulty of AC is proportional to the severity of the inflammation and fibrosis, and the risk of developing a BDI has been shown to increase in accordance with the severity of AC [9].

Table 14.1 Levels of severity for AC—according to TG18

Level I	Mild
Level II	Moderate—Conditional to the availability of advanced laparoscopic techniques
Level III	LC to be performed after GB drainage—If both the patient and facilities meet strict conditions, LC can be performed as a straightforward procedure

AC Acute cholecystitis, *TG18* Tokyo Guidelines 2018, *LC* Laparoscopic cholecystectomy, *GB* Gallbladder

The TG13 was the initial attempt to establish a complexity scale of AC based on intraoperative findings during LC. As a result, an initial expert consensus was reached by more than 400 surgeons from Japan, Korea, and Taiwan [12]. Following this initial publication, a Delphi survey was then performed. The survey consists of the opinion of 614 international surgeons when confronted with 29 scenarios that might involve the risk of BDI along with possible preventive measures [13].

14.2.2 Risk of Iatrogenic Bile Duct Injury

The incidence of BDI is considered to be 2 to 5 times higher for LC when compared to the open approach [14, 15]. Thus, it is important for the operating surgeon to identify the preoperative risk. Considering the high number of LCs performed in a single institution due to AC, it is important to promptly and adequately identify these risk factors leading up to a potentially difficult LC. Mainly, inflammatory tissue surrounding the GB affects both the correct identification of structures and their safe isolation. The stage of inflammation also plays a key role, with advance and severe inflammation affecting the visualization more than early and mild inflammation. All these factors also affect the operation time. The GB's pathological process that directly affects the complexity of the procedure includes GB wall thickening, impacted stones at the GB's neck with potential mass effect on common bile duct, duration of elevated C-reactive protein (CRP), nonvisualized GB on preoperative studies, body temperature, abscess formation, and body mass index (BMI) [16]. In contrast, the risks associated with conversion to an open approach include mostly observational and numerical variables: A GB wall thickening >4–5 mm on preoperative ultrasonography (USG), age >60 or 65 years old, male gender, AC TG18 level II/III, a contracted GB on USG, previous abdominal surgery, BMI, and American

Society of Anesthesiologists (ASA) score [16]. Furthermore, elevated white blood cells (WBCs), low albumin, high bilirubin, pericholecystic fluid, and diabetes mellitus (DM) are predictive factors associated with conversion to an open procedure [17–20]. As a final note on the timing of surgical intervention for AC, the available evidence shows that the rate of complications and the probability of conversion to open procedure increase significantly if the LC is performed more than 72 h after the onset of symptoms [21, 22]. This is especially important in diabetic and immunocompromised patients, in which the onset of intensity of symptoms is typically delayed, increasing the overall risks in these patient populations.

In summary, the level of surgical difficulty can be estimated by the aforementioned factors, principally the preoperative imaging studies, blood tests, and AC TG18 level. Nevertheless, both prolongation of the operative time and the rates for open conversion are greatly dependent on both the surgeon's skill and experience.

14.3 Surgical Management

14.3.1 Intraoperative Difficulty Indicators

In spite of the previously mentioned preoperative identifiers, the intraoperative objective findings are the main factors determining the complexity of the LC, are imperative, and are considered appropriate indicators of surgical difficulty during LC [12].

The intraoperative difficulty indicators became part of the AC TG18 practice guidelines. These indicators were the result of a multinational survey conducted in Japan, Korea, and Taiwan [12]. A total of 26 Japanese expert hepatobiliary surgeons generated a list of intraoperative findings that contribute to surgical difficulty using the nominal group technique. Subsequently, 61 experts were surveyed addressing LC experience, surgical strategy, and perceptions of 30 objective intraoperative findings. Of relevance, the objective intraoperative findings were categorized into factors related to inflammation and additional findings of the GB, and other intra-abdominal factors. The former factors were further subdivided into appearance around the GB, appearance of the Calot's triangle area, appearance of the GB, and additional findings of the GB and its surroundings. These factors were measured using a difficulty scale that ranged from 0 to 6; 0 being the easiest and 6 being the most difficult. A score ≥4 is highly suggestive of a difficult LC. Regarding the appearance around the GB, the presence of diffuse scarring tissue scored an average of 4. In regard to the appearance of the Calot's triangle area, both partial and diffuse scarring in the Calot's triangle area scored 4 and 5, respectively. Similarly, when considering the appearance of the GB, diffuse scarring in the GB bed (including atrophy of the GB with no lumen due to severe contraction) was the most prevalent finding with a score of 4. In terms of additional findings of the GB and its surroundings, five findings were identified as high indicators of a difficult LC. These included necrotic changes around the GB/Calot's triangle/GB bed, abscess formation toward the liver parenchyma, cholecystoenteric fistula, cholecystocholedochal fistula, and impacted gallstone in the confluence of the cystic duct (CD), common hepatic duct (CHD), and common bile duct (CBD); they were all graded as high-risk difficulty indicators with scores of 4, 4, 5, 6, and 5, respectively. As to the intra-abdominal factors unrelated to inflammation, anomalous bile duct, collateral vein formations due to liver cirrhosis, and inversion of the GB in its bed due to liver cirrhosis, were all given a score of 4. Figure 14.1 summarizes the most relevant difficulty risk identifiers in accordance with scoring from high to low.

14.3.2 Safe Steps

The preoperative risk stratification and planning should never be rescinded by any surgeon, regardless of their expertise and years of practice. Thus, in accordance with the Delphi consensus on how to perform a safe LC in the presence of AC, the authors propose a rather modified

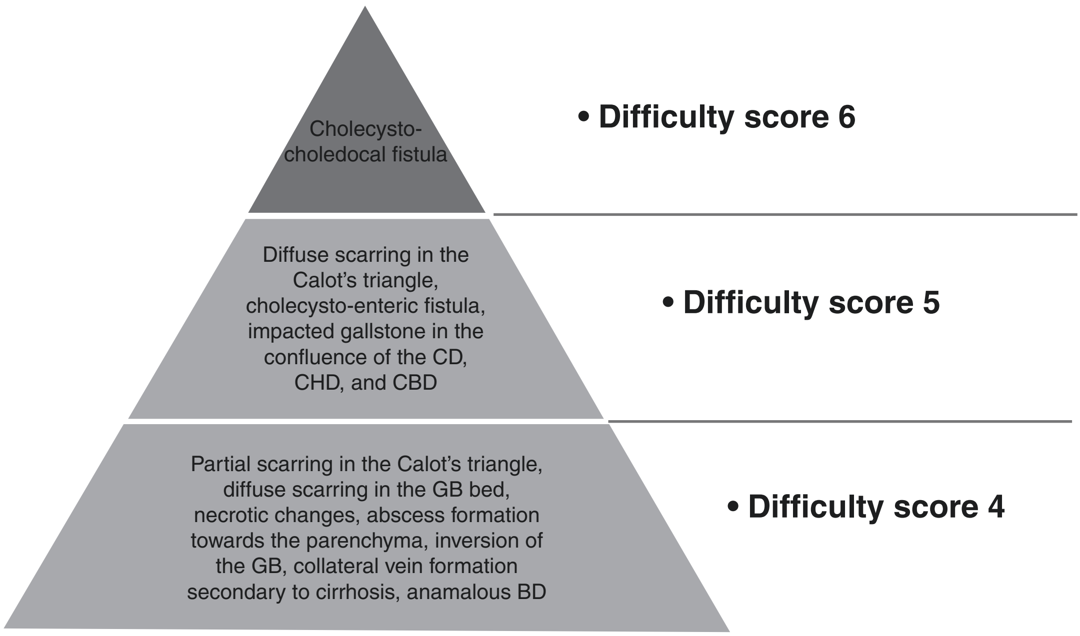


Fig. 14.1 Most commonly encountered difficulty indicators during LC

approach in views of recent and novel technologies that aid in the navigation of said procedure. Table 14.2 compares and contrasts the standard of care steps, to the new recommendations.

Evidently, the steps are seemingly different from one another. However, the proposed steps are based on both the Delphi consensus on BDI during LC and in the implementation of technologies such as fluorescence guided surgery, with the application of intraoperative incisionless fluorescent cholangiography (IOIFC) [13, 23]. The addition of IOIFC would aid in the identification of the main extrahepatic bile structures prior and during dissection with a contrast visual feedback. The advantages of this technology are obvious as often the implementation of other imaging modalities like IOC would have determined an unwanted injury already. Similarly, the CVS can be not sufficient by itself to avoid BDIs.

Initially proposed by Strasberg and colleagues, the CVS was popularized as the most commonly implemented surgical technique used to prevent BDIs [10, 24]. Although widely praised by surgeons, the CVS requires a long-time curve for residents in training and reflects in prolonged operative time [25]. Equally, the role of intraoperative cholangiography during LC continues to raise questions in regard to applicability and true benefit in the prevention of BDIs. The heterogeneous results on intraoperative cholangiography have deemed this imaging technique to be optional [24, 26]. It is important, however, to recognize that imagery feedback from surgical tools can, in fact, reduce the extent of a BDI. Perioperative cholangiography, magnetic resonance cholangiopancreatography (MRCP), laparoscopic ultrasound, and IOIFC have proven to prevent BDI, yet may require further supporting evidence [27].

14.3.3 Avoiding BDIs

Although not the focus of this chapter, operating surgeons should be knowledgeable on how to proceed in the face of a potential or an actual occurrence of a BDI. Firstly, the surgeon must be capable of identifying the type of BDI, based on Bismuth/Strasberg's classification of BDIs. The importance of appropriately classifying the type of BDI relies on the implications of the management of iatrogenic BDIs. Overall, surgical mor-

Table 14.2 Safe steps for an LC in the presence of AC

Delphi consensus steps [14]	New recommendations
Step 1 If a distended GB interferes with the field of view, decompress by needle aspiration	*Step 1* Administration of peripheral ICG
Step 2 Effective retraction of the GB to develop a plane in the Calot's triangle area and identify its boundaries	*Step 2* Exposure of the hepatoduodenal ligament
Step 3 Start dissection from the posterior leaf of the peritoneum covering the neck of the GB and exposing the GB surface above Rouvière's sulcus	*Step 3* Initial anatomical evaluation: Identification of the biliary tree structures following lysis of adhesions
Step 4 Maintaining the plane of dissection on the GB surface throughout the procedure	*Step 4* Identification of the CD and CBD junction
Step 5 Dissecting the lower part of the GB (at least one-third) to obtain the critical view of safety (CVS)	*Step 5* Identification of the CD and its junction to the GB
Step 6 Creating the CVS	*Step 6* Identification of the CHD
	Step 7 Identification of the CBD
	Step 8 Identification of the cystic artery and optional performance of an arteriography
	Step 9 Time-out before transection and reidentification of Calot's triangle structures
	Step 10 Evaluation of the liver bed and identification of accessory ducts

LC Laparoscopic cholecystectomy, *AC* Acute cholangitis, *GB* Gallbladder, *ICG* Indocyanine green, *CD* Cystic duct, *CBD* Common bile duct, *CHD* Common hepatic duct, *CVS* Critical view of safety

tality rates have been reported up to 5%, while re-stenosis rates range from 5% to 28% [28]. This should be considered prior to any type of surgical re-intervention. Additionally, these suggestions should be followed by a set of perioperative points that have been determined crucial for the avoidance of BDIs [16].

These points can be considered as a summarized confluence of the steps to follow while performing an LC, the difficulty indicators during LC, and the levels of severity for AC. The points to follow are based on tissue appearance, surgical technique, imaging tools, and bailout procedures. Figure 14.2 briefly demonstrates the highlights of said points.

Evidently, there is more to these points than just prioritizing them during the performance of the surgery. Firstly, there is an unequivocal time frame—as previously mentioned in this chapter—on the performance of surgery. LC in the setting of AC should be performed no longer than 72 h following the presenting symptoms. Failure to do so will result in extensive inflammation and fibrosis surrounding relevant structures, causing difficulties in the identification of the biliary tree anatomy and achieving CVS [29]. Secondly, meticulous surgical technique will undoubtedly provide the grounds for the prevention of BDI. The CVS must be achieved regardless of the imaging tools available in the surgical setting. Although it is a technique with limitations, it has most definitely proven its effectiveness in reducing BDI occurrences [24]. In contrast, imaging tools are dependent on the availability of them

Fig. 14.2 Critical points to prevent BDIs

Point 1 **Tissue appearance**

- LC needs to be performed prior to the development of extensive inflamation and fibrosis.

Point 2 **Surgical technique**

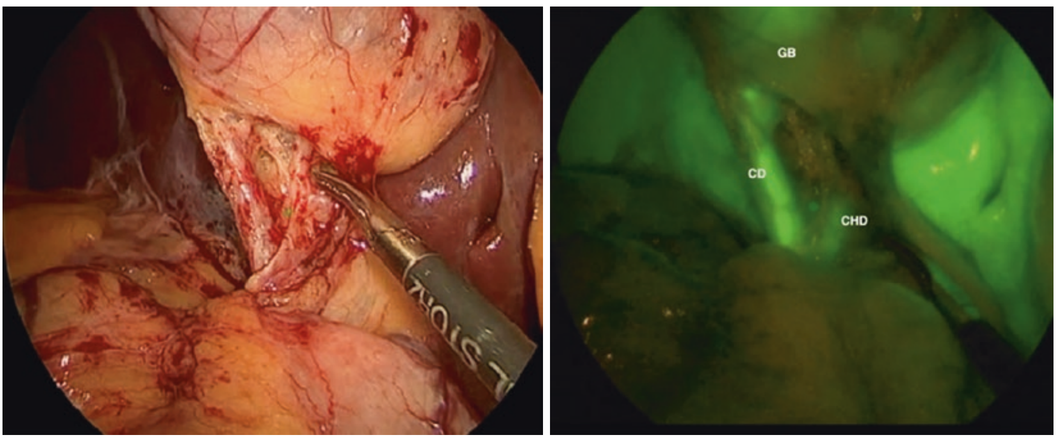
- Cephalad retraction of the GB to ensure complete view of the biliary tree anatomy - appropriate CVS.
- Prioritize on the dissection around the GB -if it is too dificult to procede, consider bail-out procedures.

Point 3 **Imaging tools**

- Intraoperative cholangiography should be performed when necessary as a standard of care procedure.
- In the presence of a dificult GB diagnosed by preoperative imaging: Consider the use of IOIFC, if available -if not, consider MRCP or laparoscopic ultrasound.

Point 4 **Bail-out procedures**

- Sub-total laparoscopic or open cholecystectomy to reduce risk of potential BDI.



Critical view of safety during an LC. Comparison between white light imaging (WLI—left) and near-infrared (NIR—right) light filter. Lysis of adhesions can be performed with NIR filter. IOIFC aids in the identification of the gallbladder and biliary structures guiding the surgeon (GB: Gallbladder; CD: Cystic duct; CHD: Common hepatic duct). Cystic artery arteriography can be performed intraoperatively by an additional administration of 3 mL of intravenous ICG

where the procedure is being performed. Further detail of aiding imaging tools is discussed later in this chapter. Lastly, bailout procedures must be considered to ensure BDI when a difficult LC has been identified. In the presence of severe fibrosis surrounding Calot's triangle, subtotal LC or open conversion must be considered [30]. Recall that objective intraoperative findings can be identified as indicators of surgical difficulty. There are still no criteria available for the conversion or performance of a subtotal LC, yet the pioneering imaging tools might rescind the need for said criterion.

14.4 Groundbreaking Alternative

Ever since LC was first described, the incidence of BDI has held a steady range between 0.3% and 0.52% [31, 32]. Mainly, the reason behind said steady incidence is the misidentification of biliary tree anatomy. Even in the presence of the CVS, both training and experienced surgeons practice LCs with the risk of developing BDIs. Imaging tools, including but not limited to, intraoperative cholangiography, MRCP, and laparoscopic ultrasound have all been developed to ease surgical performance and achieve a risk-free procedure. The literature regarding these tools is inconsistent, and although applicable in the clinical setting, these have shown to be impractical, costly, or impose an unnecessary exposure to patients. Comparatively, near-infrared (NIR) fluorescence cholangiography performed with ICG and NIR light has been described as a feasible, simple, and cost-effective technique to perform a safe LC [33].

Intraoperative incisionless fluorescent cholangiography (IOIFC) has recently emerged as a safe, simple, cost-effective technique. Furthermore, IOIFC has been proven to be statistically superior to white light in visualizing extrahepatic biliary structures during LC [23]. In the only multicenter randomized control trial available on the subject, pre-dissection and post-dissection rates favored IOIFC in the correct identification of relevant structures during LC. More so, this study revalidated the premise of IOIFC being a useful teaching tool to teach LC and hence decreasing the learning curve of this procedure [34]. In terms of performing LC in the presence of a difficult AC, the authors consider that the application of IOIFC among the already validated practice consensus will indubitably provide a greater benefit and further the risk of BDI incidence. Unfortunately, IOIFC has yet to establish itself as standard of care. Nevertheless, it is a promising tool that should be considered by the performing surgeon in the presence of either straightforward or challenging cases.

14.5 Technique

In accordance to what is steadily becoming standard of care while performing an LC, the authors have a present practice that promotes an injury-free procedure. The Delphi consensus thoroughly describes six key steps in the performance of a safe LC [13]. However, in hopes to reduce iatrogenic events associated to BDI, the use of IOIFC has been implemented into a new set of ten key steps that aim to prevent said occurrences (Table 14.2).

The technique should proceed as follows. Following induction of general anesthesia, a 2 cm supraumbilical incision is made. A Hasson cannula is placed, and a 15-mmHg pneumoperitoneum is established. Upon exploration of the abdominal cavity, three 5 mm trocars are inserted under direct vision in this order: Subxiphoid, right upper quadrant, and right mid quadrant. The gallbladder is then grasped and lifted over the liver. Fluorescent cholangiography is performed at this moment in surgery to correctly identify all relevant structures to the procedure (Table 14.2). The dissection initiates laterally, and the peritoneum surrounding the gallbladder is taken down. This is continued toward the infundibulum of the gallbladder and extended toward the liver on its medial side to allow visualization of the CD and cystic artery. The dissection is continued upon the separation of both structures. In continuance with the dissection, the cystic artery is medially approached toward the liver bed. At this point, the critical view of safety should be achieved. This view should portray overall visibility of the gallbladder and liver, in between the cystic artery and CD, just medial to the artery and under the lower border of the liver. The cystic artery is then clipped twice proximally and once distally. The CD is clipped in a similar fashion and both structures are posteriorly divided. The gallbladder is taken off the liver bed and placed in a retrieval bag for extraction, under direct vision, from the umbilicus. Irrigation continues and adequate cauterization of the liver bed.

This is a short description of the technique; however, further literature should be consulted elsewhere for detailed approach on the safe and adequate performance of an LC.

14.6 Conclusions

In the setting of AC, LC should be performed in a step-by-step manner. It is paramount for the performing surgeon to recognize all perioperative implications prior to surgery. An adequate and thorough understanding of the level of severity of the AC, the difficulty level of performing said LC, the risk indicators, safe steps, and the cardinal points for preventing BDI should provide the ideal guide for a safe LC. The authors recognize that novel imaging tools might not be present in every operative room. Thus, this chapter emphasizes the effort of the operating surgeons to prioritize the prompt recognition and following of these recommendations.

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