# Difficult Acute Cholecystitis

Treatment and Technical Issues

Isidoro Di Carlo
*Editor*

Springer

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# Foreword

The book you have in your hands holds all the knowledge that a surgeon should master to perform a cholecystectomy. This intervention is a perfect demonstration of the considerable improvement in the surgical management of patients. The approach and study of all aspects of the pathology, associated with the participation of very high level experts, make this book an essential reference. The choice of authors, all experts and often great teachers, and the choice of chapters allow readers to consolidate their knowledge and, if necessary, to develop it, especially in difficult situations, with confidence. It is Isidoro Di Carlo's success and intelligence to have made these choices and—what a very good idea—not to have hesitated to propose almost seven chapters on the same theme of difficult cholecystectomy! Consecutive reading of these seven chapters certainly brings us more information than many conferences on the subject.

At the time, admittedly distant, of my first years of surgery, a patient operated on for a gallbladder could remain hospitalized for 12 days with, of course, a drainage tube, a gastric tube, and a more or less prolonged postoperative fasting period. So, we could not rely on any morphological examination to know the specific anatomy of the patient, no strategy for the prevention of complications other than "beautiful dissection," and of course no decision algorithm nor guidelines because the surgery was considered an art.

This book shows that we have moved from a culture of gesture and technology to a culture of results and therefore safety. And yet, as rightly says Isidoro Di Carlo, this intervention—a priori and often simple—can be extremely difficult with dire consequences in the event of an error in the surgeon's judgment or strategy.

Finally, the book ends on a high note with the prevention and management of bile duct injuries. The last two chapters insist on the importance of collegiality and the multidisciplinarity of the team, which allows the necessary distance to choose an appropriate attitude, especially during the procedure.

But if you will allow me, former anatomist that I am, I wish to return to three risks of complications that may concern the simplest cholecystectomy and which are explained by anatomical concepts perfectly described or pointed out in this volume, particularly in the remarkable first chapter on anatomy.

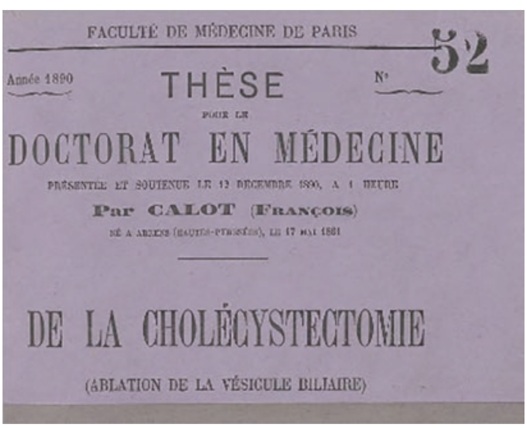
## Calot's Triangle

We must return to the historical definition of Calot's triangle because some authors have kept this name to define the modern dissection triangle at the risk of misleading a surgeon who would seek to apply it to the latter. As we know today, it is not the exposure of the Calot's triangle that ensures a safe dissection but that of the hepatocystic triangle, allowing a good critical view of safety with its three components (Strasberg): (1) the fibrous and fatty tissue is dissected off the hepatocystic (HC) triangle, (2) at least one third of the gallbladder is dissected from the gallbladder fossa/cystic plate, and (3) only two structures (cystic artery and cystic duct) are seen entering the gallbladder.

The authors of Chap. 15 said "the CVS technique is aimed especially at mobilizing the gallbladder neck from the liver in the appropriate cystic plate to obtain a circumferential identification of the cystic duct and its transition into the gallbladder." But they add: "To establish CVS, two windows need to be created during dissection of Calot's triangle: one window between the cystic artery, cystic duct and gallbladder, and another one between the cystic artery, gallbladder, and liver." Calot's triangle is stricto sensu only the first window. If you add the second window going to the liver, you get the HC triangle.

In 1890, François Calot in his thesis (Fig. 1) very precisely described a triangle.

"The common bile duct forms the right edge of the gastrohepatic omentum and the cystic duct roughly continues its direction. These two channels together describe a curved line with a concavity facing right and forward. The hepatic duct is connected to the union of the two channels, which thus forms, with the artery and the cystic duct, a kind of equilateral triangle." (Fig. 2) "The triangle is not exactly equilateral but rather isosceles, the two upper and lower sides, represented by the artery and the cystic duct being equal and only a little longer than the part of the hepatic duct which enters into the constitution of the triangle."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POUR LE

DOCTORAT EN MÉDECINE

PRÉSENTÉE ET SOUTENUE LE 12 DÉCEMBRE 1890, A 1 HEURE

Par CALOT (François)

DE LA CHOLÉCYSTECTOMIE

(ABLATION DE LA VÉSICULE BILIAIRE)

**Fig. 1** François Calot's thesis

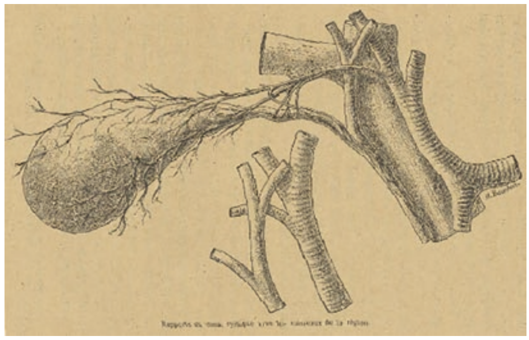

**Fig. 2** Calot's triangle: drawing of the area made by Calot himself

## Luschka's Duct

Luschka describes subvesical bile ducts in the gallbladder liver bed that may be injured, causing a postoperative bile leak, and specifies in his article that it is rare that this duct drains into the cystic duct (0.07% of cysticohepatic ducts in a series of 2012) and quite exceptional in the gallbladder (cholecystohepatic duct). It is really extremely rare to see a true picture of such a duct, and this is good because the latter is necessarily interrupted during gallbladder release, which requires a ligature or repair if it drains a significant portion of the parenchyma as in the case reported by Maeda in 2020.

There is nothing to add to the description given in the first chapter by Loukas et al.: "In 30% of the population, a small bile duct from segment 5 crosses the gallbladder fossa and is referred to as Luschka's duct. It may drain into the right hepatic duct, the common hepatic duct, or rarely the cystic duct. Since the majority of these accessory ducts are small and insignificant, any additional ducts encountered in the gallbladder fossa could be ligated safely. However, some accessory ducts may drain significant portions of the right hepatic lobe. These cases are defined as aberrant ducts, and studies have emphasized they might need to be protected during surgery."

## Anatomical Variations of Pedicle Structures Close to the Cystic Duct

The variations in biliary convergence are reviewed in the very good chapter by Martinez et al. The five anomalies according to Benson and Page are a long cystic duct with low fusion with the common hepatic duct (CHD), abnormally high fusion of cystic duct with CHD, accessory hepatic duct, cystic duct entering right hepatic duct, and finally the cholecystohepatic duct which is, as we have seen, exceptional. These structures must be recognized.

However, some structures, the most dangerous, are missing (Fig. 3). Figure 3a shows a downward slide of the right anterior (or posterior) hepatic duct; Fig. 3b shows a low bifurcation and therefore a cystic duct that empties into the right duct, with the risk of mistaking the left duct for the common bile

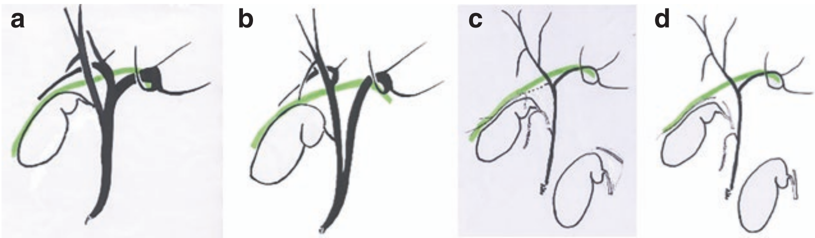


**Fig. 3** Anatomical variations of pedicle structures close to the cystic duct

duct (CBD); and finally, Fig. 3c and d show two different connections of a true Luschka's duct, which can drain a more or less important part of the liver and is not protected by the dissection of the Calot's triangle alone.

For the sake of completeness, let us remember that the position of the arteries and especially that of the right hepatic artery can also be a proven risk. In Chap. 11, the authors also perfectly describe risky situations: "One common variation occurs when the right hepatic artery runs within the lower end of the Calot's triangle in a tortuous course referred to as caterpillar or Moynihan's hump. This variation can have an incidence as high as 50%. A Moynihan's hump is clinically relevant as the cystic artery is significantly shorter in these patients. As a result, the right hepatic artery could be misidentified as the cystic artery and could result in erroneous ligation…. In other cases, the right hepatic artery has been found to take another aberrant course in which it passes anterior to the bile duct or even posterior to the portal vein."

We hope that these reminders, which only underline points already mentioned in the various chapters, will at least reduce biliary accidents. These occurrences may seem rare as their incidence is close to 0.3%. However, at 600,000 cholecystectomies per year in the United States, this rate represents 1800 cases each year.

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# Preface

Acute cholecystitis is one of the most common emergencies in the context of acute care surgery. In recent decades, surgical societies and expert groups have produced guidelines that have sought to guide surgical behavior in relation to these diseases. However, despite the advice of many experts, treatment of this disease remains a challenge, especially for the complications that can arise from related surgical procedures. To describe all the tricks that can be used to cure the difficult cases of acute cholecystitis, without complications, represents the main goal of this book. It is important to remember that it is a benign disease, and strong complication cannot be accepted both by surgeons and patients. For this reason in these pages, residents and young surgeons will find all the eminent advice that can be used daily to treat safely all patients affected by this disease.

All the surgeons that have contributed to this textbook are preeminent scientists. With their personal experience, they have contributed to clarify all the aspects of difficult acute cholecystitis. I am indebted to all the authors for their valuable work.

I met during my career skilled surgeons expert in a dedicated field of surgery, but I met only one surgeon who is able to operate all the organs of the abdomen with extraordinary skills both using open and laparoscopic approaches. In my opinion Prof. Brice Gayet is one of the best surgeons of the world, and I am really honored and grateful that he has accepted to write a foreword to this book.

Catania, Italy — Isidoro Di Carlo

# Contents

# Anatomy of the Gallbladder and Biliary Tract

1

Vincent Courant, Michael Montalbano, Anna Zurada, Agnieszka Zurada-Zielińska, Jerzy Gielecki, and Marios Loukas

## 1.1 Introduction

Cholecystitis accounts for up to 10% of cases of abdominal pain worldwide. For most patients with acute cholecystitis, the preferred treatment is surgical excision of the gallbladder, commonly via laparoscopic cholecystectomy. Other treatment options are open surgery, percutaneous cholecystostomy tube, antibiotics, and supportive therapy. In the U.S alone, around 600,000 people are subjected to cholecystectomy annually [1]. Anatomical variations with clinical significance are found in 20% of laparoscopic cholecystectomies. These mostly include variations in the cystic artery (10%), cystic duct (4%), right hepatic artery (3%), and the gallbladder itself (2%) [2]. Misinterpretation of the exposed anatomy contributes to complications, which occur in 1–6% of laparoscopic cholecystectomy cases. Common iatrogenic injuries are directed toward the biliary tree and surrounding blood vessels, with such injuries possibly causing severe morbidity and life-threatening situations. As a result, it is crucial for surgeons to have a clear understanding of the underlying anatomy, as well as be aware of possible anatomical variations to ensure the best results for their patients.

## 1.2 Anatomy of the Gallbladder

The gallbladder is a flask-shaped, hollow organ that may vary in size and shape. In adults, the gallbladder usually measures 7–10 cm in length with a capacity of up to 50 mL. The organ is usually found resting on the gallbladder fossa, which is located on the inferior surface and marks the caudal limit of Couinaud segments 4 and 5 (Fig. 1.1), although this location may change between individuals [1]. However, there are cases of intrahepatic gallbladder where the organ lies within the liver parenchyma or under

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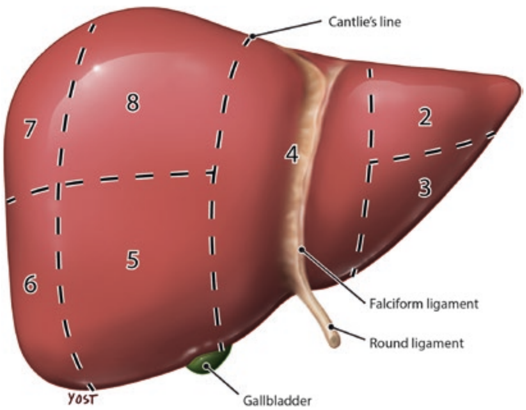


**Fig. 1.1** Liver segments and their relation to the gallbladder. (Printed with permission Katie Yost, 2020)

the hepatic capsule at the inferior part of the right lobe. This variation can generate difficulties with dissection as well as heighten the probability of intraoperative hepatic injury. "Floating gallbladders," where the organ hangs freely and is only attached to the cystic mesentery, have also been found [2]. This particular variation may predispose the patient to gallbladder torsion [3]. On rare occasions, additional ectopic locations of the gallbladder have been found to occur at the lesser omentum, falciform ligament, transverse mesocolon, suprahepatic, abdominal wall, retrorenal space, left lower abdomen, and adjacent to the inferior vena cava [2].

The gallbladder is typically separated into three components: the fundus, the body, and the neck.

The neck is defined as the posterosuperior limit of the gallbladder connected to the cystic duct. It is typically 5–7 mm in diameter and takes an S-shaped curve. The neck is located close to the porta hepatis, which is a 5-cm deep fissure extending transversely underneath the left portion of the right hepatic lobe. The porta hepatis is located within the hilum of the liver and contains, from posterior to anterior, the portal vein, the right and left hepatic arteries, as well as the right and left hepatic ducts. A reflection of the peritoneum covering the inferior surface of the liver forms a sleeve around these structures referred to as the hepatoduodenal ligament or free edge of the lesser omentum. A fold of peritoneum connects the hepatoduodenal ligament to the peritoneal layers around the gallbladder, forming the cholecystoduodenal ligament. Of note, on the medial surface of the neck there is a spiral groove that may run along the spiral valves of the cystic duct. The valves are made of several crescentic folds projecting into the lumen of the duct and may be absent in 2% of the population [2].

On the lateral side of the neck, there may be an outpouching referred to as Hartmann's pouch. This expansion is often measured via sonographic imaging to find evidence of dilation or presence of stones. While the pouch may vary in size, a larger Hartmann's pouch can obscure the cystic duct, common hepatic duct, and cystic artery. Similarly, a large stone in a Hartmann's pouch causes an erosion into the bile duct in a condition referred to as Mirizzi's syndrome. These cases can create major difficulties during cholecystectomy.

The body represents the central portion of the gallbladder between the neck and fundus. The body is typically in contact with the liver at the gallbladder fossa, which is usually found anteriorly in relation to the second part of the duodenum and to the right of the transverse colon. The fundus is the most distal part of the gallbladder and forms the anteroinferior margin. It is lateral to the body and often contacts the anterior abdominal wall at the costal margin [4]. The fundus usually folds back on the body of the gallbladder. The gallbladder lumen is widest at the junction of the body and fundus and gets narrower as it travels toward the neck with the most rapidly narrowing segment called the infundibulum.

In some cases, the fundus and body might be separated by an external cleft leading to the formation of a "double" or "bilobed" gallbladder. The second gallbladder is referred to as "accessory" if it drains into a separate cystic duct. An accessory gallbladder may vary in size and may either be separated from its counterpart or contained together within a single peritoneal envelope. The gallbladder might also display a diverticulum along its length, measuring up to 5 cm. In rare cases (0.07%), the gallbladder is entirely absent, with the rest of the biliary tree anatomy remaining normal. In these cases, ultrasound imaging may fail to make the correct diagnosis of absent gallbladder, which can lead to patients undergoing unnecessary surgery [2].

The shape of the gallbladder may also vary. There have been cases of septate gallbladder, which are constituted with the presence of a septum that partly or entirely divides the gallbladder into chambers that are empty via a single cystic duct. The gallbladder might also display a diverticulum along its length, measuring up to 5 cm.

## 1.3 Biliary Tree

### 1.3.1 Cystic Duct

The cystic duct is one of the main structures that need to be identified during cholecystectomy. The cystic duct measures from 2 to 4 cm in length and 2 to 3 mm in width. However, size may vary, and a cystic duct larger than 5 mm could be mistaken for the common bile duct. It is also important to note that about 20% of the U.S. population has a cystic duct measuring less than 2 cm, which will make ligations more difficult. The duct commonly travels posteriorly and to the left of the gallbladder neck. The duct usually follows a tortuous course until it meets the common hepatic duct, from the right lateral aspect to form the common bile duct at a variable site ranging from the right hepatic duct to the ampulla of Vater region (Fig. 1.2). Less commonly, the cystic duct may also be S-shaped, curved with acute flexures, or straight.

The cystic duct has been found to exhibit several anatomic variations. The cystic duct junction with the common hepatic duct may occur at a more inferior point in the free margin of the lesser omentum. The cystic duct has also been observed taking different routes as it travels away from the gallbladder. In 75% of cases, the cystic duct joins the common bile duct at an acute angle. It has also been observed to run parallel to the right side of the common hepatic duct in 20% of cases. Rarely, the cystic duct may take a spiral course posterior to the common hepatic duct before entering on its left side (5%) [2].

Since such variations are possible, ligating the cystic duct at its connection with the common bile duct may predispose patients to biliary tree injury. It is helpful to remember that, even with its variations, the cystic duct rarely runs posterior to the duodenum. Therefore, ductal structures that pass behind the duodenum are more likely to be common bile ducts [1]. Another way that may distinguish the two structures is that the cystic duct usually will not have vessels traversing its surface, while the common bile duct does [4].

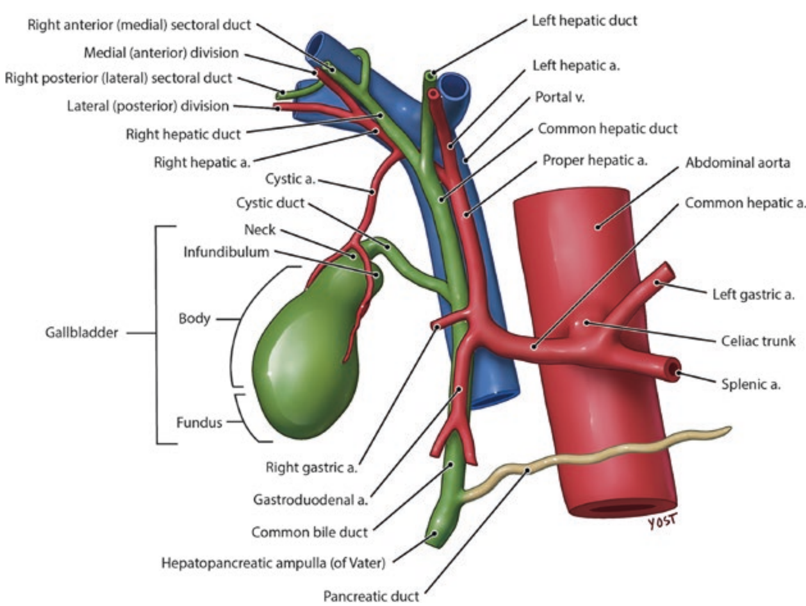


**Fig. 1.2** Anatomy of the gallbladder and biliary tree. (Printed with permission Katie Yost, 2020)

The cystic duct may also display aberrant drainage to the left and right hepatic duct, right intrahepatic sectional duct, or drain into the left side of the common hepatic duct. Accessory intrahepatic ducts draining into the cystic duct may also occur. Additionally, the cystic duct may vary numerically as it may be completely absent or present as a double cystic duct, although they are exceedingly rare. As a result, if two ducts are seen entering the gallbladder surgeons should keep a high suspicion that one of the ducts is part of another structure related to the biliary tree [1].

### 1.3.2 Hepatic Bile Duct

In the liver parenchyma, bile canaliculi fuse to form segmental bile ducts, each draining one hepatic segment. The segmental ducts then combine in a specific pattern to form sectional ducts. Ducts from segments 6 and 7 form the right posterior sectional duct, and ducts from segments 5 and 8 form the right anterior sectional duct. The right hepatic duct arises from the meeting of the right anterior and right posterior sectional ducts at a variable intrahepatic point (Fig. 1.2).

Segments 2 and 3 contribute segmental ducts that coalesce to form the left lateral section duct, which then unites with the duct from segment 4 to form the left hepatic duct. The right and left hepatic ducts meet to form the common hepatic duct near the medial end of the porta hepatis.

The right hepatic duct takes a short vertical course of about 1 cm, while the left hepatic duct travels horizontally for 3 cm along the inferior border of segment 4 (Fig. 1.1). The right hepatic duct system has a higher frequency of variation than the left ductal system. The right hepatic duct may be absent in 15% of cases. In this variation, the common bile duct is formed by a triple confluence from the right anterior, right posterior, and left hepatic ducts. Additionally, a right sectoral duct may join the left hepatic duct in 15% of cases. Occasionally, a right segmental duct may join the common hepatic duct below the normal meeting point. This variation may cause the right segmental duct to be misidentified for the cystic duct during surgery. Consequently, if a structure similar to the cystic duct is to be divided, careful dissection toward the infundibulum should be performed to verify that it is directly connected to the gallbladder [5].

Rarely, the duct from segment 5 or the right posterior sectoral duct drains directly into the cystic duct or the gallbladder itself. Also, infrequently, some branches of the right posterior sectional duct may enter the distal bile duct supraportally and the remaining branches infraportally.

The left intrahepatic ductal system may vary in the arrangement of the segmental duct from segment 5. This segmental duct may drain into the bile ducts from segments 2 or 3, the right anterior sectoral duct, or the common hepatic duct. The bile ducts from segment 1 usually join the origin of the left hepatic duct but may drain into both hepatic ducts.

Finally, there might be multiple accessory hepatic ducts. A more detailed review on accessory ducts will be covered later in this chapter.

### 1.3.3 Common Bile Duct

The common bile duct is on average between 6 and 8 cm long and travels infero-posteriorly within the right border of the lesser omentum. It travels anterior and to the right of the portal vein, as well as to the right of the hepatic artery. The common bile duct then runs posterior to the first part of the duodenum and to the left of the gastroduodenal artery. It passes posterior to the head of the pancreas, forming its retropancreatic portion. Finally, the common bile duct passes through the sphincter of Oddi to enter the second part of the duodenum at the major papilla, where it may be palpated during surgery [4, 5]. Of note, the pancreatic duct forms a common channel with the common bile duct in 85% of cases; however, the two ducts may enter the duodenum separately. The common bile duct may also vary numerically. In some cases, the common bile duct is completely absent. In this rare variation, the left and right hepatic ducts drain into the gallbladder while the cystic duct directly joins to the duodenum [2]. Conversely, there can be a "double" common bile duct where the ducts run parallel to each other and are separated by a septum.

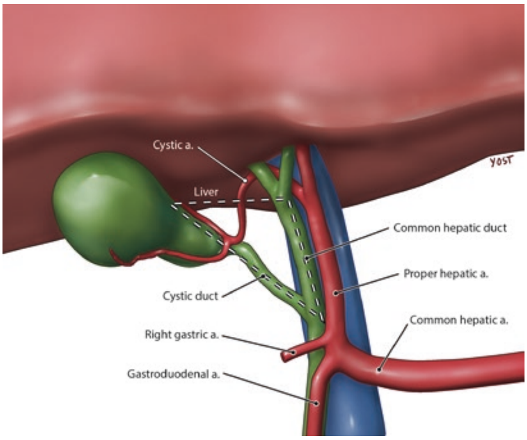


**Fig. 1.3** Calot's triangle. (Printed with permission Katie Yost, 2020)

### 1.3.4 Calot's Triangle

Calot's triangle, or the hepatocystic triangle, was first described in 1891 and represented the triangular space formed by the cystic duct, the common hepatic duct, and the cystic artery [6]. Today, the upper border is now commonly referred to as the inferior edge of hepatic segment 4, while the lateral and medial borders represent the cystic and common hepatic bile ducts, respectively (Fig. 1.3). The triangle usually contains the cystic artery, lymphatics, the cystic lymph node of Lund, small cystic veins, autonomic nerves, and loose connective tissue. Calot's triangle may also contain any accessory hepatic ducts and blood vessels draining into the gallbladder's surrounding anatomy.

This triangular space is clinically important as it is dissected during cholecystectomy to identify and ligate the cystic artery and duct. As a result, it is crucial to be aware of the anatomical structures contained within Calot's triangle to avoid unnecessary damage to the surrounding structure.

### 1.3.5 Accessory and Aberrant Ducts

The normal biliary anatomy exists in only about 50% of the population [5]. Several accessory ducts are detailed in the biliary drainage system of the liver. The accessory ducts most frequently encountered in a cholecystectomy are those that drain portions of the right lobe, as they remain near the gallbladder. These ducts are usually miniscule and travel through Calot's triangle. Then, they usually join the common hepatic duct where the right and left hepatic ducts merge. In some cases, the cystic duct was found to join an accessory duct prior to its connection with the common hepatic duct. Rarely, a cholecystohepatic duct has been found to join the gallbladder directly. Occasionally, there may be multiple ducts draining segment 4 into the left duct, or the segment 4 duct may join the segment 3 duct before uniting with the segment 2 duct [2].

In 30% of the population, a small bile duct from segment 5 crosses the gallbladder fossa and is referred to as Luschka's duct. It may drain into the right hepatic duct, the common hepatic duct, or rarely the cystic duct [2]. Since the majority of these accessory ducts are small and insignificant, any additional ducts encountered in the gallbladder fossa could be ligated safely [1]. Occasionally, there might also be multiple ducts draining segment 4 into the left hepatic duct, or the segment 4 and 3 ducts may unite before joining the segment 2 duct [2]. However, some accessory ducts may drain significant portions of the right hepatic lobe. These cases are defined as "aberrant" ducts, and studies have emphasized they might need to be protected during surgery [1]. Ligation of these ducts may lead to severe biliary stasis or leak, and the size of the duct can indirectly indicate its functional importance. It is recommended that any injury to a duct over 3 mm in width should be drained into a Roux-en-Y anastomosis. This surgical technique aims at relieving biliary obstruction by creating an anastomosis between the duct and jejunum via choledochojejunostomy. Alternatively, a cholangiogram could be performed through the duct to evaluate the amount of liver drainage and identify whether it is accessory or aberrant.

Detailed classification of iatrogenic bile duct injuries following cholecystectomy needs to include clinically relevant data on every injury pattern since this will influence surgical treatment and outcome [7, 8]. There have been numerous categorizations of common bile duct injury

(BDIs), since Bismuth first introduced them in 1982 [9]. Bismuth classification ranked BDI based on its location in the biliary duct. Since the adaptation of laparoscopic cholecystectomy, more recent classifications have also focused on size, bile leakage, vascular involvement, mechanism of BDI, and severity of injury. A recent classification was introduced by Stewart-Way, whose most common injury type involves the transection and excision of a variable length of the common bile duct and always includes the junction between the common and cystic ducts [10].

## 1.4 Imaging of the Gallbladder and Biliary Tree

The normal anatomy of the gallbladder may be demonstrated using the imaging techniques that have been developed to examine diseases of the gallbladder. These include oral cholecystography, sonography, scintigraphy, CT scan, and MRI [11]. Right upper quadrant ultrasound is the preferred initial modality when investigating pain that is suggestive of cholecystitis. The normal gallbladder should be visualized in nearly all patients after a 10-h fast. In patients with cholecystitis, imaging may include the presence of stones, distension of the lumen, wall thickening (>3 mm), a positive sonographic Murphy sign, pericholecystic fluid, and a hyperemic wall on color doppler. Detailed information of the biliary anatomy can be obtained by relying on techniques such as magnetic resonance cholangiography or intraoperative cholangiogram. Both of these techniques use a contrast agent that accumulates in the gallbladder and bile duct system. These methods are particularly useful for the diagnosis of biliary tree obstruction by evidence of bile duct dilation and filling defect.

## 1.5 Vasculature and Lymphatics

### 1.5.1 Cystic Artery

The arterial supply of the gallbladder arises from the cystic artery. The cystic artery originates from the right hepatic artery and is commonly found within Calot's triangle (Fig. 1.3). The cystic artery then runs anterior to the cystic duct and posterior to the common hepatic duct. As the artery approaches the gallbladder neck, it separates into anterior and posterior branches that ultimately meet on the gallbladder surface. Multiple smaller branches may also supply the hepatic ducts and the superior portion of the common bile duct. Close attention must be made to these vessels during surgery as injury to the artery may lead to severe bleeding.

Additionally, the cystic artery is variable in origin. It could arise from the common hepatic artery, left hepatic artery, and gastroduodenal artery. Rarely, the cystic artery has also been found to originate from the right gastric, celiac, superior pancreaticoduodenal, and superior mesenteric arteries. As seen in these variations, the cystic artery usually crosses the common bile duct anteriorly.

Finally, a double cystic artery has been found to occur in 2–15% of cases. In these cases, the accessory artery has been described arising from the right hepatic artery, common hepatic artery, and left hepatic artery [1, 4]. If the cystic artery branches from the common hepatic or the left hepatic arteries, the cystic artery may cross the bile duct anteriorly, predisposing patients to iatrogenic injury.

### 1.5.2 Ductal Arteries

The biliary tree is supplied by a network of blood vessels originating from multiple surrounding sources. Blood vessels to the common bile duct run along its entire length. The main contributors to this network of vessels are coming from the retroduodenal branch of the gastroduodenal artery as it nears the upper boundary of the duodenum. Other common sources are the cystic and right hepatic arteries. A retroportal artery has also been found to originate from the celiac or superior mesenteric arteries, the vessel usually runs superior-posteriorly along the portal vein before joining the retroduodenal artery. Rarely, the retroportal artery has also been seen joining the right hepatic artery. The hepatic ducts are supplied by multiple fine blood vessels arising from segmental arteries contained within the Glissonian sheath, which is a layer of connective tissue enveloping the hilar structures inside the liver.

### 1.5.3 Right Hepatic Artery

The right hepatic artery rises from the bifurcation of the common hepatic artery, usually to the left of the hepatic hilum. The vessel typically courses posterior to the bile duct and anterior to the portal vein until it joins the right pedicle in the Calot's triangle. One common variation occurs when the right hepatic artery runs within the lower end of the Calot's triangle in a tortuous course referred to as "caterpillar" or "Moynihan's" hump. This variation can have an incidence as high as 50% [1]. A Moynihan's hump is clinically relevant as the cystic artery is significantly shorter in these patients. As a result, the right hepatic artery could be misidentified as the cystic artery and could result in erroneous ligation. It is recommended to divide the cystic artery close to the gallbladder wall in order to avoid confusion with other possible blood vessels. In other cases, the right hepatic artery has been found to take another aberrant course in which it passes anterior to the bile duct or even posterior to the portal vein. In addition, an accessory or replaced right hepatic artery from the superior mesenteric artery may occur in approximately 17% of individuals. In these cases, the right hepatic artery courses posterior to the portal vein and the inferior end of the common bile duct.

### 1.5.4 Venous Drainage

The venous drainage of the gallbladder arises from a system of multiple fine veins. Vessels exiting the superior surface of the body and neck typically enter the liver to join segmental portal veins. The rest of the gallbladder vein system forms small cystic veins that join the intrahepatic drainage either directly or indirectly via veins from the hepatic ducts. Rarely, cystic veins may drain into the right portal branch. There have been only a few reports of clinically significant veins injury involving the portal vein after biliary tree surgery.

### 1.5.5 Lymphatics

A multitude of lymphatic vessels arises from the plexuses of the gallbladder and cystic duct.

The lymphatic drainage of bile ducts diverges into two pathways. The superior pathway involves lymph nodes along the cystic duct, hepatic artery, and celiac plexus. In contrast, the inferior pathway involves the nodes along the cystic lymph nodes, located superiorly to the cystic duct and embedded within Calot's triangle. This pathway also drains into the anterolateral aspect of the portal vein, the posterior pancreas, and the aortocaval region. Chyle leakage is an extremely rare complication after cholecystectomy.

### 1.5.6 Nerve Supply

The hepatic plexus innervates the gallbladder and biliary tree. In addition, the common bile duct also receives branches from the pyloric branch of the vagus nerve. Pain sensation arising from these structures is commonly referred to as the epigastric region, while stimulation of the overlying somatic peritoneum will lead to pain in the right upper quadrant. The Murphy's sign is elicited in patients suffering from acute cholecystitis by having the patient hold a deeply inhaled breath while conducting palpation of the right subcostal area. If pain occurs, Murphy's sign is positive. While nerve injury during cholecystectomy is a very rare occurrence, a few cases of unilateral phrenic nerve palsy have been reported in the literature. It has been hypothesized that this might be due to pneumoperitoneum that leads to stretching of the phrenic nerve [12].

## 1.6 Conclusion

The anatomy of the gallbladder and biliary tract is complex and displays a wide range of variations. Detailed knowledge of the anatomy is needed for surgeons to avoid potential complications and perform a successful procedure.

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# 2 Pathophysiology and Diagnosis of Acute Calculous Cholecystitis

Alberto R. Ferreres

## 2.1 Introduction

Gallbladder ailments have been affecting humans for thousands of years, as proved by the fact of gallstones found in Egyptian and Chinese mummies. In 1909, an Egyptian mummy was presented to the Museum of the Royal College of Surgeons in London, with a preserved liver and a gallbladder, containing 30 gallstones. The mummy came from Thebes and belonged to a twenty-first dynasty priestess (circa 1500 BC) and was donated by Dr. Elliot Smith, a well-known Egyptologist and anatomist. The gallbladder was described as "large and containing many spherical calculi" (1).

Alexander the Great is believed to have died on July 11,323 BC at age 34 due to peritonitis resulting from the perforation of an acute cholecystitis, fueled by alcohol consumption and abundant intake. In 1867, John Bobbs performed the first cholecystostomy on a 31-year-old lady who survived until the age of 77 in Indianapolis. Fifteen years later, Carl Langenbuch performed in Berlin the first cholecystectomy in a 35-year-old male patient (2).

Acute calculous cholecystitis (ACC) accounts for 3–11% of hospital admissions and carries a mortality of about 0.8% (3). ACC represents more than 90% of all cases of acute cholecystitis, the remaining include acalculous, xanthogranulomatous, and other variations of acute cholecystitis. The gold standard treatment of ACC is laparoscopic cholecystectomy, but its timing (early vs. delayed) is also a matter of discussion.

Although most patients with cholelithiasis remain asymptomatic for long periods, 1 to 4% of those patients per year suffer biliary colics (4, 5). ACC eventually may develop in about 20% of those symptomatic patients if left untreated (6). Nonetheless, most patients with ACC have had previous episodes of biliary colic pain; but for some, ACC may represent the initial episode. In some cases, ACC may coexist with choledocholithiasis, acute cholangitis, or acute biliary pancreatitis. Around 60% of patients with ACC are women; however, ACC develops more frequently in men and tends to be more severe (7). Patients suffering from diabetes are also more prone to develop ACC.

ACC represents the most frequent complication of patients with diagnosis of choledocholithiasis. Gallstone disease incidence is a major world health problem which undoubtedly is expanding. The best method to investigate the real incidence of biliary gallstones is screening ultrasonography, since it is far superior than autopsy findings and clinical diagnosis, which requires biliary symptoms only present in 20% of those individuals with gallstones. The frequency of cholecystectomy, mostly performed in a laparoscopic approach, has a very limited relationship to the prevalence of the disease and

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is more related to the surgeon's driven practice as well as patient access to surgical care (8). In developed countries, 10–15% of white adults carry gallstones. It is estimated that in the USA about 15% of the population are gallstone carriers, with a higher incidence in the Hispanic population than in non-Hispanics. In that country, 6.3 million males and 14.2 million women between 20 and 74 years have gallbladder stones (9). A very high prevalence has been described in American native Indians, such as the Pima group in Arizona. The same applies to original Indian populations in South America. The prevalence of gallstones in the Hispanic population of Latin America (Central and South America) is higher, similarly to native populations in the same areas. In these populations, genetic risk factors lead to lithogenic bile and gallstone early in life (less than 30 years) resulting in gallstone prevalence rates of more than 50% at 50 years of age in both men and women (10). In Europe, the Multicenter Italian Study on Cholelithiasis (MICOL) informed an overall incidence of gallstones of 18.8% in females and 9.5% in males (11). In south east Asia, the prevalence is lower, but usually located in the bile ducts and associated with parasitic infestations (12).

In the West, about 70% of gallstone carriers possess cholesterol gallbladder stones, with a cholesterol content of more than 50%, meanwhile 30% have black pigment gallbladder stones. In eastern Asia, there is a very high incidence of pigment stones lodged in the bile ducts and being responsible for causing severe cholangitis. Nonetheless, in these countries the incidence of cholesterol gallstones has been steadily increasing in the last years, presumably due to the changes in the diet.

Ethnicity is a major determinant of the following facts: cause of the disease, type of stone/s, and location in the biliary tract system. In developed countries, most of the gallstones (around 85%) are predominantly of cholesterol composition, where the remainder 15% are black pigment calculi, due to calcium bilirubinate. Cholesterol and black pigment stones are formed within the gallbladder lumen, but in the first case the starting point is represented by the liver production of supersaturated bile with cholesterol, which tends to precipitate in the gallbladder. The excess secretion of mucin together with an impaired gallbladder motility keep these crystals, aggregating to them other materials and turning them into macroscopic stones (13).

Gallstones may be classified according to their location and composition (Fig. 2.1, see Addenda). The location may be: extrahepatic (choledocholithiasis) where the stones may be present in the

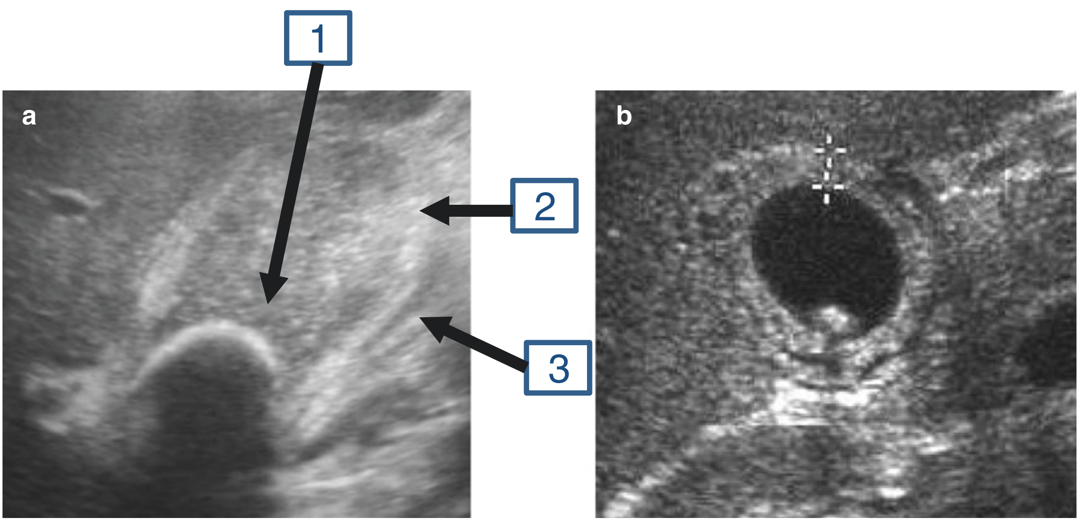


**Fig. 2.1** (**a**): 1. Impacted gallstone + sludge. 2. Wall thickening. 3. Pericholecystic fluid. (**b**): Gallbladder wall with thickening of its layers and an impacted gallstone

gallbladder and/or in the common bile duct, or intrahepatic (hepatolithiasis). Stones in the common bile duct may be either primary (originated de novo in that conduct, and usually pigment stones) or secondary, due to migration from the gallbladder and, typically, of cholesterol. Black pigment stones also develop in the gallbladder, but consist of bilirubin polymers (calcium bilirubinate) and are typically associated with advanced age, liver cirrhosis, cystic fibrosis, and hematologic conditions with increased erythrocytes' destruction (sickle cell anemia, chronic hemolytic states).

Bile duct stones may originate in the gallbladder and get there due to migration or otherwise develop primarily in the biliary system. In the Western world, the risk of concomitant common bile duct stones, which migrate from the gallbladder, is estimated in 10–15% and is usually compounded by cholesterol. But choledocholithiasis may develop primarily due to strictures and subsequent inflammation and infection with the appearance of brown pigment stones. In southeastern Asia, pigment stones are predominant, composed by calcium bilirubinate, fatty acids, cholesterol, and mucin (glycoproteins primarily from bacterial biofilms). They tend to aggregate in the common bile duct or in the intrahepatic bile ducts. Infection by bacteria but mostly by parasites (*Clonorchis sinensis*, *opisthorchis species*, and *fasciola hepatica*) as well as stasis represent key factors (8).

Risk factors for gallstone formation are multifactorial (14):

- Constitutional: Represented by age, female gender, genetics, and ethnicity. These are not able to be changed or modified.
- Environmental or exogenous: Include the following factors, which represent modifiable conditions:
  - Dietary factors: Mostly linked with cholesterol gallstone formation, including high carbohydrate/high calories intake, high glycemic upload, low fiber intake.
  - Metabolic aspects: Also linked with cholesterol gallstone formation. Physical inactivity, diabetic or prediabetic conditions, obesity, nonalcoholic fatty disease.
  - Increased enterohepatic bilirubin circulation: Liver cirrhosis, Crohn's disease (both for cholesterol and pigmentary stones), ileal resections, and bariatric procedures (for pigmentary stones).
  - Underlying chronic disease: Cystic fibrosis, spinal cord injuries, some colon conditions are associated with increased risk of gallstones development.
  - Medications: Hormone replacements, octreotide, fibrates, calcineurin antagonists.
  - Alterations in the motility of the gallbladder.

## 2.2 Pathogenesis of Gallstones

### 2.2.1 Cholesterol Stones

Bile is a yellow-brown to dark green fluid whose composition is more than 90% water. Bile contains bile salts, cholesterol, and phospholipids as well as little amounts of proteins and inorganic salts. In humans, bile is produced by the liver and stored in a concentrated fashion in the gallbladder. It serves as a surfactant, emulsifying the lipids in the digestive tract. Bile salt anions are hydrophilic on one side and hydrophobic on the other, tending to aggregate around droplets of lipids to form micelles, with the hydrophobic sides towards the fat and the hydrophilic facing outwards.

The organization of cholesterol gallstones is the consequence of a failure in the homeostasis of cholesterol concentration in the bile. The increase in the liver production of biliary cholesterol has been considered the primary pathophysiologic defect in human cholelithogenesis, followed by abnormal secretion rates of bile salts and phospholipids and thus inducing the supersaturation of cholesterol in the gallbladder bile.

There are five primary defects which play a major role in the organization and formation of cholesterol gallstones (Table 2.1, see Addenda):

**Table 2.1** Primary defects for cholesterol gallstone formation

| Cholesterol gallstones |
|---|
| 1. Genetic factors and lith genes |
| 2. Liver cholesterol hypersecretion into bile |
| 3. Alterations in the motility of the gallbladder |
| 4. Rapid phase transitions of cholesterol in bile (with precipitation of cholesterol crystals) |
| 5. Intestinal factors: |
| • increased absorption of cholesterol |
| • slow intestinal motility |
| • dysbiosis |

#### 2.2.1.1 Genetic Factors and Lith Genes

A genetic predisposition to gallstone formation seems to be clearly evident (15). The discovery of the lithogenic Lith 1 and Lith 2 genes in mice's chromosomes 2 and 19, respectively associated with quantitative trait locus (QTL) analysis—a powerful genetic study technique—confirmed the genetic role in alterations ending in gallstone formation.

Genome-wide association study (GWAS) has allowed the study in humans, leading to the discovery of two major variants: ABCG5-R50C and ABCG8-D19H, which have been associated with gallstones formation in German, Chilean, Chinese, and Indian populations (16). Nonetheless, less than 25% of the risk of cholesterol gallstones is determined by genetics (17).

#### 2.2.1.2 Liver Cholesterol Hypersecretion into Bile

Although cholesterol secreted into bile recognizes its origin from liver synthesis, reverse cholesterol transport, and chylomicrons, the contribution of each pathway is not yet absolutely clear. Estrogens enhance the formation of cholesterol gallstones by stimulation of the liver synthesis and the production of cholesterol as well as the reduction in the production of bile salts. These mechanisms are the ones responsible for the higher prevalence of stones in females than in males.

#### 2.2.1.3 Alterations in the Motility of the Gallbladder

The emptying of the gallbladder tends to be impaired before gallstones are detected, giving a clinical picture of biliary dyskinesia. This phenomenon is due to the fact of the absorption of large amounts of cholesterol by the epithelial cells of the gallbladder's wall from the supersaturated bile. Cholesterol in excess is transformed to esters and stored in the mucosa and lamina propria, originating changes in the sarcolemmal membranes with further disruption of cholecystokinin I receptors' signaling cascade as well as the alteration of the signal transduction mediated by G proteins (18).

#### 2.2.1.4 Rapid Phase Transitions of Cholesterol in Bile (with Precipitation of Cholesterol Crystals)

The secretion of cholesterol into the bile depends on the balance of the liver's cholesterol input and output. Cholesterol crystal nucleation is considered the first and earliest step in cholesterol gallstone formation and depends on the relative amounts of cholesterol, phospholipids, and bile salts. Although cholesterol solubility in watery solutions is very little, the situation is completely different amidst gallbladder bile. This increase in solubility is due to the incorporation of cholesterol in mixed micelles, together with bile salts and phospholipids, the most representative being phosphatidylcholine.

Supersaturation of the bile occurs when either too much cholesterol or not enough bile salts and phosphatidylcholine molecules are secreted to permit the complete solubilization of micellar cholesterol. The cholesterol in excess may be stored in vesicles or in cholesterol crystals (19). The organization of these crystals is believed to happen from vesicles supersaturated with cholesterol, in the two following stages:

(a) Small unilamellar supersaturated vesicles tend to gather or fuse into larger multilamellar crystals (cholesterol crystal nucleation).
(b) Subsequent phase separation of cholesterol crystals (20).

Wang and Carey studied the cholesterol crystallization pathways and sequences in human gallbladder bile and were able to describe the equilibrium bile salt, phospholipid, and cholesterol ternary phase diagram, which permits to predict the behavior of the three components when present in different proportions (21). Three factors strongly affect the balance of the bile salt–phospholipid–cholesterol ternary phase diagram, with potential alterations of the cholesterol crystallization: the bile concentration, the higher hydrophobicity of bile salts and the type phospholipids, and the composition of their acyl chains.

1. Intestinal factors: are represented by the increased absorption of cholesterol, a slow intestinal motility, and the alterations in gut microbiota.

The small bowel absorbs cholesterol from the diet intake and reabsorbs the cholesterol present in the bile, depending upon the expression of sterol transport proteins (16). Small and large bowel dysbiosis occurs in cholesterol gallstone patients and may be affected by toxins introduced with the food intake.

### 2.2.2 Pigment Stones

(a) Black pigment stones: Their primary component is calcium bilirubinate, while other components are calcium carbonate and calcium phosphate joined to mucin glycoproteins. In normal conditions, most bilirubin, the breakdown product of hemoglobin, is conjugated in the liver to bilirubin monoglucuronide and subsequently to water-soluble bilirubin diglucuronide, highlighting the fact that unconjugated bilirubin is poorly soluble in water. In case of hemolysis, biliary excretion of bilirubin is very much increased, with the risk of precipitation of calcium bilirubinate. This mechanism explains the high prevalence of these type of stones in chronic hemolytic disorders (22).
(b) Brown pigment stones: In contrast to the black, these are mostly developed in the lumen of the bile ducts. Their primary composition is calcium salts of unconjugated bilirubin and different amounts of cholesterol and proteins. They are associated with bile stasis and chronic bacterial infection of the bile ducts by *Escherichia coli*, *Bacteroides spp*, *Clostridium spp* and parasites like *Opisthorchis viverrini*, *Clonorchis sinensis*, *Ascaris lumbricoides* (Table 2.2, Addenda). Bacteria produce β glucuronidase, phospholipase A, and bile acid hydrolase which leads to an increase in the amounts of unconjugated bilirubin, palmitic and stearic acids, and unconjugated bile acids, which can join with calcium and thus form stones. Parasites may stimulate stone formation by the calcified overcoat of the parasite egg, which may serve as the nucleus of the future stone with the deposit of calcium bilirubinate (23).

**Table 2.2** Factors for the formation of brown pigment stones

| |
|---|
| Genetic factors |
| Liver hypersecretion of bilirubin |
| Bile stasis |
| Bacterial infection |

## 2.3 Pathophysiology of ACC

The primary cause of acute cholecystitis is obstruction. Of all individuals who have gallstones, only 1–3% will undergo an acute episode. Other obstructive causes include: primary tumors of the gallbladder or the biliary tract, polyps, parasites, metastatic tumors, or nodes in the vicinity of the gallbladder neck (24).

The extended gallbladder outlet obstruction by a stone is the initial and main factor leading to an ACC. The process corresponds to the physical obstruction of the gallbladder by a gallstone, which may be located at the neck or in the cystic duct. The following sequence of pathophysiologic steps is described in the production of an episode of ACC (Table 2.3, Addenda): the obstruction leads to distention and an increased gallbladder pressure, taking into account the fact that the progression to acute cholecystitis is determined by two main factors: (a) the degree of

**Table 2.3** Steps in the development of calculous acute cholecystitis

| |
|---|
| Obstruction at the gallbladder's neck |
| ↓ |
| Increased endoluminal pressure |
| ↓ |
| Venous congestion, compromised blood irrigation, alterations in lymphatic drainage Ischemia of the mucosa |
| ↓ |
| Release of inflammatory mediators: prostaglandins I2 and E2 |
| ↓ |
| Localized mucosal trauma |
| ↓ |
| Lysosome release of phospholipase |
| ↓ |
| Conversion of lecithin to lysolecithin |
| ↓ |
| Wall thickening + edema, vascular congestion and intramural hemorrhage |
| ↓ |
| Mucosal ulcers with focal areas of wall necrosis |

obstruction and (b) the duration of the obstruction by the stone. Meanwhile the obstruction is partial and the duration short, the patient will most probably experience a biliary colic, but if the obstruction is complete and the duration long, an acute cholecystitis episode will develop. In this case, if the patient does not receive immediate treatment, the clinical picture will tend to progress and increase the severity of its evolution with a higher incidence of complications. The persistence of the obstruction leads to a sustained increase in the gallbladder endoluminal pressure, leading to venous congestion, a compromise in the blood irrigation, and the lymphatic drainage with mucosal ischemia. It is important to note that the inflammatory response and the release of its mediators (prostaglandins I2 and E2) generate the release of phospholipase from the lysosomes, which aids in the conversion of lecithin into lysolecithin, via enzymatic hydrolysis, within the supersaturated bile in the gallbladder lumen. Lysolecithin is a potent detergent and very harmful for the mucosa (25). The gallbladder wall may suffer from necrosis and gangrene, achieving a gangrenous or necrotizing cholecystitis.

Regarding the role of bacteria, this fact does not play neither an initial nor a major role in ACC, but it has been recognized that secondary infection may complicate up to 50% of the cases (26). Bacteria implicated in ACC are usually present in the bile before the onset of the disease, since bacterial growth is present in 20% to 70% of patients. They include:

(a) Gram negative bacilli (*Escherichia coli*, *Klebsiella spp*, *Enterobacter spp*).
(b) Gram positive cocci (*Enterococci*).
(c) Anaerobes (Bacteroides, *Clostridia spp*, *Fusobacterium spp*).

A major Achilles' heel is represented by the limitations of microbial cultures, situation that may be improved by the use of next-generation sequencing (27). The overgrowth of gas-producing bacteria within the gallbladder lumen may lead to emphysematous cholecystitis.

Histologically, infiltration of neutrophilic leukocytes, microabscesses, and secondary vasculitis will be the usual findings. Secondary bacterial infection, due to delay in diagnosis or inappropriate initial antibiotic treatment, may result in gallbladder empyema with accumulation of pus, perforation with localized or generalized peritonitis, and even sepsis (13). Other complications are liver abscess and intra-abdominal collections.

There are some specific forms of acute cholecystitis that need to be distinguished from ACC: (a) xanthogranulomatous, (b) emphysematous, (c) acalculous, and (d) torsion, due to inherent, acquired, and other physical causes.

## 2.4 Diagnosis of ACC

The diagnosis of ACC is based on the clinical presentation and imaging. Although ACC is a common disease for patients presenting in the Emergency Department, its diagnosis represents a major challenge for clinicians and surgeons, in order to decide the best treatment and management strategy. The cornerstone of a correct and precise diagnosis consists of the evidence of an acute inflamed gallbladder with stones in its lumen, preventing the passage of bile to the cystic duct and the main biliary duct due to impacted calculi.

The diagnosis of ACC is based on the clinical presentation and physical examination, laboratory, and imaging studies. Nonetheless, the gold standard for diagnosis is the confirmation of the presence of a stone obstructing the gallbladder infundibulum or the cystic duct together with the pathological examination of the specimen, performed through a cholecystectomy, usually in a minimal invasive approach.

Most patients who present with ACC have symptoms of right upper quadrant pain, but many times the pain may be referred in different locations as well as irradiation. When the inflammation worsens, the pain tends to be localized in the right upper quadrant. The patients may also refer a history of biliary colic or dyspepsia or even a previous diagnosis of cholelithiasis, but sometimes the acute presentation is the initial one. Nausea, vomiting, and anorexia are usually described in the acute episode.

The most typical physical sign is the presence of abdominal pain, usually in the upper abdomen and the right upper quadrant. The examination may evidence tenderness or Murphy's sign in the right upper quadrant; this sign was described in 1903 as a sign of cholelithiasis (28). A palpable mass is usually present in about 25% of patients after more than 24 h of symptoms. In occasions, ACC can derive in sepsis and organ failure, usually when a gangrenous or emphysematous cholecystitis is present. The additional presence of choledocholithiasis should be ruled out, since this situation may preclude a somewhat different approach.

According to the Tokyo Guidelines 2013 (29), the diagnostic criteria are based on the following three aspects:

(a) Local signs of inflammation: (1) Murphy sign, (2) right upper quadrant mass/pain or tenderness.
(b) Systemic signs of inflammation: (1) fever, (2) elevated protein C, (3) elevated white blood cell count.
(c) Imaging findings, characteristic of acute cholecystitis.

Ultrasonography should be considered as the first option as imaging modality (30). The typical and pathognomonic findings include: thickening of the gallbladder wall (5 mm or more), pericholecystic fluid, and ultrasonographic Murphy's sign (abdominal tenderness when the probe is pushed against the right upper quadrant or the palpable gallbladder). The simultaneous presence of these three signs is definitive for the diagnosis of acute cholecystitis. Other findings include an enlarged and distended gallbladder, an impacted stone, and debris echo (Figs. 2.1 and 2.2, Addenda_2). According to a meta-analysis published by Shea et al. (31), the diagnostic capability of ultrasonography for acute cholecystitis achieves a sensitivity of 88% and a specificity of 80%.

Ultrasonography is also useful when an emphysematous cholecystitis is suspected since an irregular thickening of the gallbladder wall and imaging of a ruptured gallbladder may be noted.

The suspected diagnosis of ACC includes one item in (a) and one item in (b), meanwhile

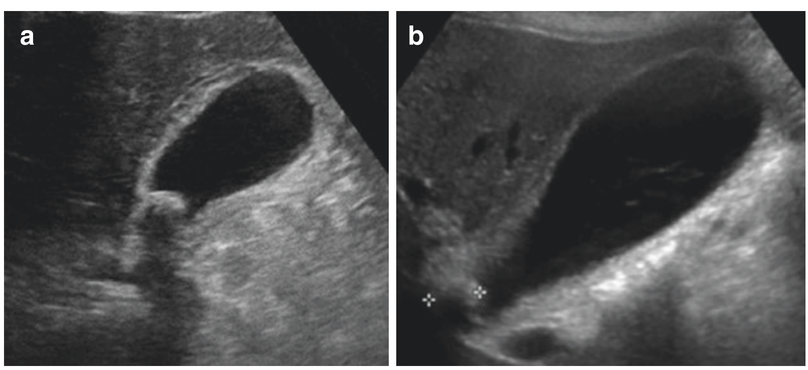

**Fig. 2.2** (**a**): Distended gallbladder with impacted gallstone. (**b**): Distended gallbladder with impacted gallstone

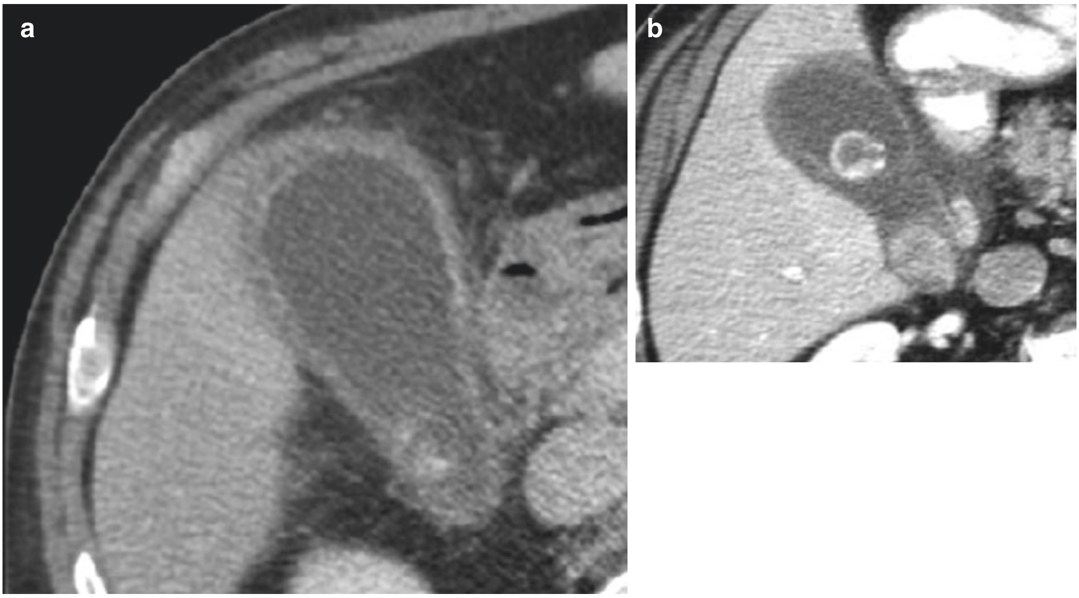


**Fig. 2.3** (**a**): CT scan, showing a distended gallbladder with impacted gallstone. (**b**): CT Scan, with distended gallbladder with impacted stone and another one in its lumen

a definitive diagnosis of ACC includes one item in (a) and one in (b) plus (c). The level of serum bilirubin may be increased due to several factors: compression of the common bile duct by the inflamed infundibulum or the presence of contemporary common bile duct stones.

Some remarks should be added to these guidelines: some patients may present with few or minimal systemic symptoms and hence, underdiagnosed, and the use of protein C levels is seldom used for the diagnosis of ACC in many countries (32). From the point of view of laboratory tests, there are no specific ones for performing a diagnosis of ACC. The World Society of Emergency Surgery guidelines for ACC also recommend the use of clinical, laboratory, and imaging findings for the diagnosis (33).

Contrast-enhanced CT scans are usually not requested in the emergency setting, exception made in those conditions where a differential diagnosis needs to be ruled out. Some of the findings are: gallbladder distention, pericholecystic fat stranding, gallbladder wall thickening, subserosal edema, mucosal enhancement, transient focal enhancement of the liver adjacent to the gallbladder, pericholecystic fluid collections, pericholecystic abscess, gas collection within the gallbladder (Fig. 2.3, Addenda_2). It is recommended to rule out gangrenous cholecystitis (Fig. 2.4, Addenda_2) as well as emphysematous cholecystitis, where the main findings include gas in the wall or lumen, intraluminal membranes, irregular or absent wall, abscess/es, Fig. 2.5 Addenda_2 (30).

The use of magnetic resonance cholangiography maybe useful in the emergency setting to rule our common bile duct stones and hence, the chance of acute cholangitis. At a time, the use of HIDA scan (with 99 Tc-HIDA cholescintigraphy) was considered the most accurate test for the diagnosis of acute cholecystitis, with a sensitivity of 97% and specificity of 87% (34). The gallbladder was usually visualized within 30 min and the absence of the radiotracer uptake by 4 h was considered positive for cystic duct obstruction. Identification of the radiotracer in the pericholecystic space is suggestive of perforation. But since the availability of emergency ultrasound, HIDA scan is considered unnecessary.

The Tokyo Guidelines 2013 also collaborated in setting guidelines for establishing the severity of ACC in three grades (29):

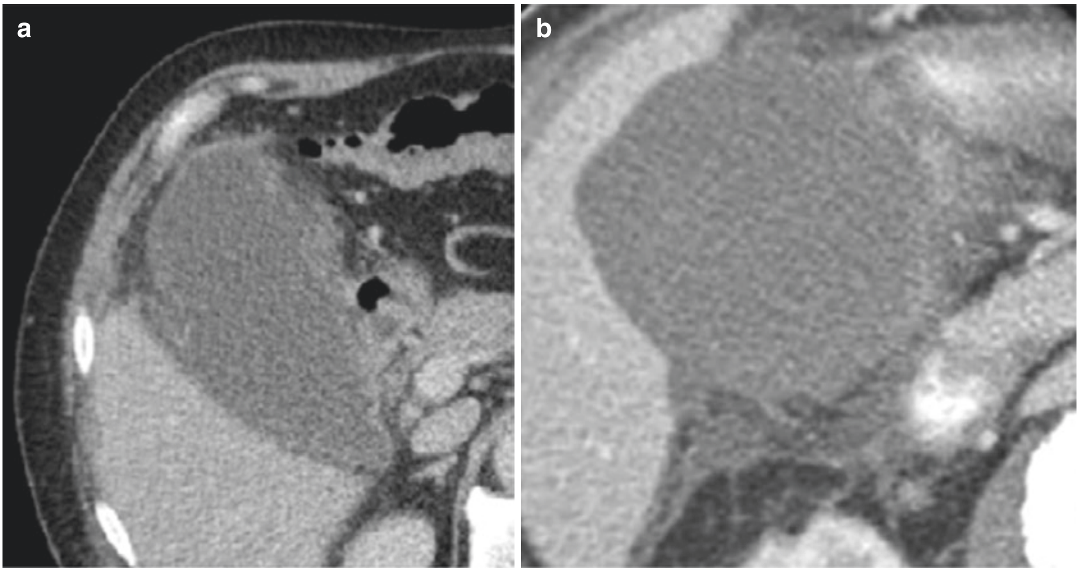


**Fig. 2.4** (**a**, **b**): CT scan Gangrenous cholecystitis

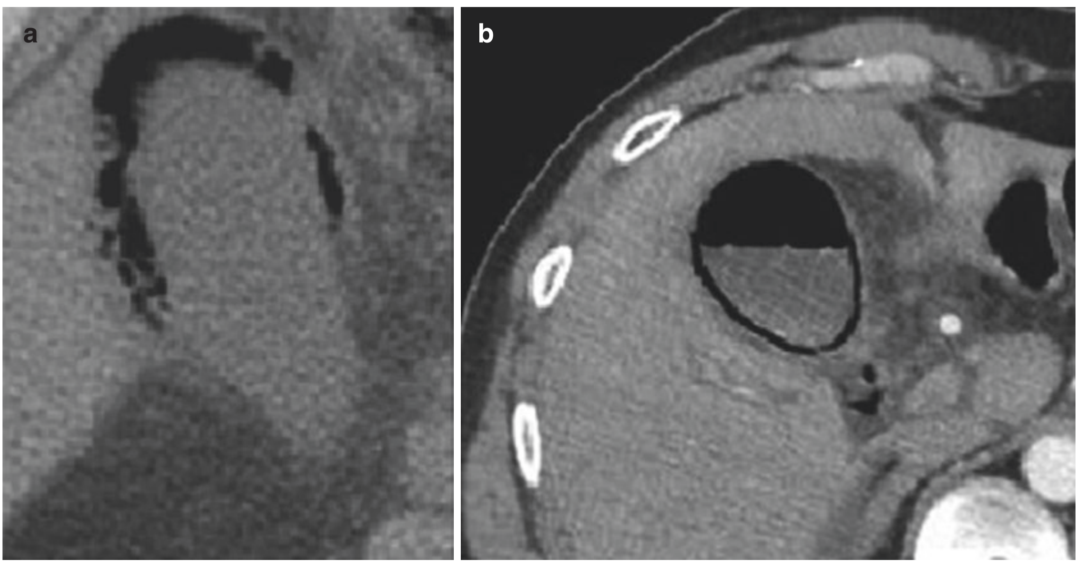


**Fig. 2.5** (**a**, **b**): CT scan Emphysematous cholecystitis

- Mild (Grade I): Acute cholecystitis in a healthy individual with no organ dysfunction, mild inflammatory changes in the gallbladder, making cholecystectomy a safe and low-risk operative procedure.
- Moderate (Grade II): Acute cholecystitis in which the degree of acute inflammation is likely to be associated with increased operative difficulty in performing cholecystectomy (WBC > 18,000/mm$^3$, palpable tender mass, duration of complaints >72 h and/or suspicion of local complications gangrenous cholecystitis, pericholecystic abscess, hepatic abscess, biliary peritonitis, emphysematous cholecystitis).

– Severe (Grade III): Associated with organ dysfunction (cardiovascular, neurological, respiratory, renal, liver, and hematologic) and mandating intensive care with respiratory and circulatory support.

There are other grading scales for severity of acute cholecystitis, such as the one proposed by the American Association for the Surgery of Trauma, based on anatomic variables using clinical, imaging, operative, and pathologic criteria to assess the severity of acute cholecystitis in 5 Grades, excluding physiologic parameters. Grade 1 corresponds to acute cholecystitis; Grade 2, gangrenous or emphysematous cholecystitis; Grades 3 to 5 describe gallbladder perforation with local contamination, abscess or fistula and generalized peritonitis, respectively (35, 36). The Parkland score relies solely on the intraoperative macroscopic findings (37).

**Keypoints**

- ACC may eventually develop in about 20% of symptomatic patients when left untreated.
- The primary cause of ACC corresponds to the physical obstruction of the gallbladder by a gallstone, which may be located at the neck or in the cystic duct.
- Bacterial infection does not play neither an initial nor a major role in ACC, but secondary infection may complicate up to 50% of the cases.
- The diagnosis of ACC is based on the clinical presentation and imaging, being ultrasonography the most widely used in the emergency setting.
- Contrast-enhanced CT is useful in clinical conditions where a differential diagnosis needs to be ruled out.

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# 3 Pathophysiology and Diagnosis of Acute Acalculous Cholecystitis

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## Abbreviat ions

AAC Acute acalculous cholecystitis
ACC Acute calculous cholecystitis

## 3.1 Introduction

Acute acalculous cholecystitis (AAC) is an acute necro-inflammatory infection of the gallbladder with a multifactorial pathogenesis, in the absence of cholelithiasis, sludge, or cystic duct obstruction on diagnostic imaging [1]. The condition was first described by Duncan in 1844. It accounts for approximately 2–15% of all cases of acute cholecystitis [1, 2] and is associated with high morbidity and mortality rates.

## 3.2 Epidemiology

AAC occurs in 0.2–0.4% of all critically ill patients [3] with predisposing multifactorial risk factors (Table 3.1). AAC has a predominance in elderly, as well as a male predominance ranging 40–80% and even more [4, 5], affecting patients much older and more predominantly of male sex than acute calculous cholecystitis (ACC) [6, 7]. However, AAC may also occur in young and middle-aged outpatient healthy individuals [2]. In children, AAC represents 50–70% of all cases of acute cholecystitis [8]. The incidence of AAC in outpatients is not well defined. Up to 77% of patients diagnosed with AAC during hospitalization may in fact have the onset at home without evidence of acute illness or trauma, but with significant vascular disease in up to 72% of these cases [9]. Although this would indicate that the actual incidence in outpatients may be in fact much higher than acknowledged, it may be also possible that some of these patients in this condition may have been misdiagnosed as AAC due to failure to reveal gallstones or microcrystals.

## 3.3 Etiology

AAC occurs more frequently as a complication of severe acute conditions (polytrauma, severe burns, shock, aortic dissection, or non-biliary operations—especially aortic surgery, acute myelogenous leukemia) [10–12]. AAC is also often associated with chronic conditions such as diabetes mellitus, cardiovascular disease, chronic kidney disease, vasculitis, acquired immunodeficiency syndrome, malignant tumors, bone marrow transplantation, and long-term total parenteral nutrition [13, 14]. Patients with cancer are at risk for AAC, including metastasis to the porta hepatis, therapy with interleukin-2, and

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**Table 3.1** Risk factors and infections predisposing to acalculous cholecystitis

| Risk factors for acalculous cholecystitis | Infections predisposing to acalculous cholecystitis | Risk factors that warrant broad empiric antimicrobial coverage |
|---|---|---|
| Systemic diseases:<br>– Acute myelogenous leukemia<br>– Diabetes mellitus<br>– End-stage kidney disease<br>– Immunosuppression<br>– Infections/Sepsis | Bacteria:<br>– *Coxiella burnetiid*<br>– *Campylobacter jejuni*<br>– *Salmonella species* (S. enterica, S typhi)<br>– *Brucella species*<br>– *Leptospira species*<br>– *Mycobacterium tuberculosis*<br>– *Vibrio cholerae* | Factors associated with mortality:<br>– Age > 70 years<br>– Comorbidities (e.g., liver disease, malignancy, chronic malnutrition)<br>– Immunocompromising conditions (e.g., poorly controlled diabetes mellitus, chronic high-dose corticosteroid use, other immunosuppressive agents, neutropenia, advanced AIDS, B or T leukocyte deficiency)<br>– Factors related to acalculous cholecystitis: high severity (i.e., sepsis); extensive peritoneal involvement or diffuse peritonitis; delay in initial intervention (source control) >24 h; inability to achieve adequate debridement or drainage control |
| Cardiovascular diseases:<br>– Coronary heart disease<br>– Heart failure<br>– Aortic dissection<br>– Hypotension<br>– Cholesterol emboli<br>– Vasculitis | Fungi:<br>– *Candida species*<br>– Isospora | |
| Iatrogenic factors:<br>– Cardiopulmonary resuscitation<br>– Mechanical ventilation<br>– Nonbiliary surgery<br>– Cystic duct obstruction by a percutaneous transhepatic catheter in the bile duct<br>– Medications (e.g. opiates, sunitinib)<br>– Multiple transfusions<br>– Total parenteral nutrition<br>– Bone marrow transplantation | Parasites:<br>– *Ascaris lumbricoides*<br>– *Echinococcus granulosus*<br>– *Plasmodium species*<br>– *Cryptosporidium* | |
| Surgical emergencies:<br>– Burns<br>– Major trauma | Viruses:<br>– Cytomegalovirus<br>– Epstein-Barr virus<br>– Flavivirus<br>– Hepatitis A and B<br>– Dengue virus | Factors associated with antibiotic-resistant bacteria:<br>– Nosocomial infections<br>– Travel related: travel to areas with high rates of antibiotic-resistant organisms within the few weeks prior to infection onset; antibiotics received during travel<br>– Known colonization with antibiotic-resistant organisms |
| HPB diseases:<br>– Ampullary stenosis<br>– Choledochal cyst<br>– Hemobilia<br>– Metastases involving portal vein | Miscellaneous:<br>– Snake bites | |
| Miscellaneous:<br>– Pregnancy<br>– Childbirth | | |

lymphokine-activated killer cells for metastatic disease [15]. Local conditions that may often lead to AAC include dehydration, bile stasis, gallbladder dysmotility, or ischemia; systemic conditions that commonly lead to AAC include inflammation mediators [16], systemic bacterial (gram-negative or anaerobic) or viral (EBV, hepatotropic virus) infections, and sepsis [17, 18]. AAC usually develop as a secondary infection of the gallbladder during systemic sepsis, such as disseminated candidiasis, leptospirosis, chronic biliary tract carriers of typhoidal and nontyphoidal Salmonella, cholera, and tuberculosis [19–24], less often malaria, brucellosis, and dengue fever [25–27]. AAC due to extrahepatic biliary obstruction may have infectious, such as ascariasis and echinococcal cysts [28, 29], or noninfectious causes, such as haemobilia, choledochal cyst, ampullary stenosis, or percutaneous transhepatic catheter drainage [30–32]. Rare causes for AAC are photodynamic therapy for duodenal lesions or snakebite [33, 34].

AAC has been reported in 0.7–0.9% of patients following open abdominal aortic reconstruction, in 0.5% of patients following cardiac surgery, and in as many as 4% of patients who have undergone bone marrow transplantation [4, 35, 36].

## 3.4 Pathogenesis

### 3.4.1 Gallbladder Wall Ischemia

Although not completely understood, the pathogenesis of AAC is related to blood stasis and ischemia of the gallbladder wall, usually related to hypoperfusion, that lead to a local inflammatory response that induces necrosis of the gallbladder wall [14, 37]. Gallbladder ischemia is central to the pathogenesis of AAC. Hypoperfusion is due to hypotension (e.g., heart failure), dehydration (e.g., fever), and vasoactive drug administration [37].

Prolongation of ischemia has been associated with increased mucosal phospholipase A2, superoxide dismutase activities, and increased mucosal lipid peroxide content, associated with high rates of gallbladder necrosis and perforation [35, 38]. Gallbladder specimen arteriography reveals marked differences between ACC and AAC [39]: ACC is correlated with arterial dilatation and extensive venous filling, while AAC is correlated with multiple arterial occlusions and minimal-to-absent venous filling, underlining the key role of vascular occlusion and microcirculatory disruption in the pathogenesis of AAC. Additionally, reperfusion injury may worsen the ischemic injuries of the gallbladder wall [40].

An interrelationship between ischemia and stasis can result in hypoperfusion [41]. In this model, bacterial invasion of ischemic tissue becomes a secondary phenomenon [41].

### 3.4.2 Bile Stasis

Another cause of AAC is thought to be bile stasis and increased lithogenicity of bile, proven in both experimental and clinical studies [8]. Hospitalized patients often have bile stasis due to multiple factors including dehydration, absence of oral intake that leads to impaired enterohepatic circulation, long-term total parenteral nutrition, and impaired gut metabolism. Volume depletion leads to bile concentration, thus the bile becomes thick bile or sludge and, in correlation with the absence of a stimulus for gallbladder emptying, may obstruct the cystic duct. Moreover, the use of opioid analgesics induces the spasm of the sphincter of Oddi as adverse effect, increasing the intraluminal bile duct pressure, promoting bile stasis. Bile stasis may also be prompted by mechanical ventilation with positive end-expiratory pressure that also reduces portal perfusion by increasing hepatic venous pressure [42]. Ileus is also thought to induce in bile stasis, but experimental results are conflicting.

Critically ill patients are more predisposed because of increased bile viscosity due to fever and dehydration and because of prolonged absence of oral feeding resulting in a decrease or absence of cholecystokinin-induced gallbladder contraction.

Bile stasis may be aggravated by total parental nutrition [43]. Parenteral nutrition is associated with gallstone formation, as well as AAC, in both adults and children. During long-term total parental nutrition, the incidence of AAC may be as high as 30% [44], while gallbladder “sludge” occurs in 50% of these patients at 4 weeks and is omnipresent at 6 weeks [45]. Neither cholecystokinin administration, to stimulate gallbladder emptying, nor enteral alimentation can completely prevent AAC among critically ill patients [46].

Bile stasis may alter the chemical composition of bile, which may induce gallbladder mucosal injury. For example, lysophosphatidylcholine may induce acute cholecystitis in animal models with identical histopathological features to that of human AAC [47]; lysophosphatidylcholine has potent effects on gallbladder structure and functional water transport across mucosa [47]. Other bile compounds (e.g., beta-glucuronidase) have also been implicated in the pathogenesis of AAC [44].

### 3.4.3 Vasoactive Mediators

Vasoactive mediators also play a key role in the pathogenesis of AAC. Bacterial infection is most likely a secondary event, while the phenomena of primary importance seems to be the host response to splanchnic ischemia/reperfusion injury or gram-negative bacteremia. Intravenous injection of *Escherichia coli* lipopolysaccharide, a potent stimulus of inflammation and coagulation, produces AAC in several mammalian species [48, 49]. Human gallbladder mucosal cells stimulated in vitro with the same compound inducing the production of eicosanoids and platelet-activating factor [50]. AAC can also be induced by injecting plant polyphenols that activate factor XII directly and generate spasm of the cystic artery [51]. Platelet-activating factor induces splanchnic hypoperfusion in sepsis and other low-flow states [52]. The inflammation appears to be mediated by pro-inflammatory eicosanoids, as it is inhibited by nonspecific cyclooxygenase inhibitors [49].

In AAC, endothelial injury, gallbladder ischemia, and stasis lead to concentration of bile salts, gallbladder distension, and gallbladder wall necrosis. The majority of patients with AAC have multiple risk factors (Table 3.1) [36, 53–55].

### 3.4.4 Infection

In some cases, specific primary infections predispose to AAC (Table 3.1). More often, however, these infections cause a cholangiopathy without cholecystitis. Once AAC is established, secondary infection with enteric pathogens, including *Escherichia coli*, *Enterococcus faecalis*, *Klebsiella spp.*, *Pseudomonas spp.*, *Proteus spp.*, and *Bacteroides fragilis* and related strains is common [56]. Perforation occurs in severe cases [57]. AAC is associated with a higher incidence of gangrene and perforation compared to ACC.

Bacteremia is one of the major causes of morbidity and mortality in the ICU [58]. Early diagnosis of bacteremia and prompt initiation of antibiotic therapy improve the clinical outcomes in critically ill patients [14].

The incidence of bacteremia has increased over time despite the availability of suitable antibiotic therapy [59]. The most common bacterial species associated with AAC, identified by blood and/or bile cultures, are gram-negative *Enterobacteriaceae*, such as E. coli and *Klebsiella pneumoniae* [60], [61], followed by *Enterococcus species*, *Staphylococcus spp.*, *Streptococcus spp.*, and *Candida spp.* [14]. Particularly, AAC associated with acquired immunodeficiency syndrome (AIDS) or other immunosuppressive conditions may be due to opportunistic infections such as microsporidia, *Cryptosporidium,* or cytomegalovirus [62].

In pediatric patients, AAC occurs in young children and neonates, as well as older children [63]. Common precipitant factors are dehydration, acute bacterial infections, viral diseases, such as hepatitis, upper respiratory tract infections [64], and portal lymphadenitis with extrinsic cystic duct obstruction. Recent studies suggest that the pathogenesis may be similar to that in adults [63].

## 3.5 Clinical Manifestations

The clinical presentation of AAC varies based on the severity of illness and underlying predisposing conditions (Table 3.1). Early diagnosis is the key to improve prognosis because of the fast progression of AAC due to gangrene and perforation, with dismal prognosis [37]. AAC has to be suspected in a critically ill patient, often intubated and sedated, presenting sepsis or unexplained fever, jaundice, abdominal discomfort, or high transaminases (not justified for other reasons), especially in postoperative setting [6].

The presentation may be similar to ACC, with fever, severe right upper quadrant pain with tenderness at palpation, and positive Murphy's sign [6], sometimes presenting with a palpable right upper quadrant mass and/or crepitus (due to emphysematous cholecystitis) and rarely jaundice [9]. Murphy's sign is operator-dependent and involves an alert and cooperative patient; when present, is indicative of gallbladder inflammation. Presentation characterized by recurrent biliary symptoms for months or years usually has gallstone-related disease or functional gallbladder disorder. The presentation may be insidious; therefore, patients may have sepsis, shock, and peritonitis at presentation due to complications including gallbladder necrosis, gangrene, or perforation.

Jaundice typically results from sepsis-related cholestasis, partial biliary obstruction due to inflammation expanding to the common bile duct or due to extrinsic compression of the common bile duct by a phlegmon (Mirizzi-type syndrome).

Nowadays, the diagnosis rate of AAC is increasing due to several factors, such as increased number of severe forms, enhanced awareness on behalf of the medical staff, improved imaging techniques, and consideration of AAC in the differential diagnosis of complications in patients with major comorbidities [37].

As AAC occurs frequently in critically ill patients, it is important to recognize this condition:

- The potentially critically ill patient: is sweaty, anxious, pale, agitated, or confused; responds to moderate stimulation only (loud voice, physical prodding); uses the respiratory accessory muscles at a respiratory rate of 20–30 or under 8; has the heart rate over 100, the systolic blood pressure under 90, and the urinary out is under 0.5 ml/kg/h.
- The critically ill patient: has a severe general status; is dehydrated, unresponsive, or poorly responsive neurologically; has the respiratory rate under 8 or over 30, the heart rate under 50 or over 150, the systolic blood pressure under 60, oliguria or anuria. These patients might not withstand surgery when the Charlson Comorbidity Index (CCI) is at least 6 and the American Society of Anesthesiologists physical status classification (ASA-PS) is at least 3 (patients with severe systemic disease, with one or more moderate to severe diseases, that leads to significant functional limitations with one or more organ dysfunctions) [65–67].

## 3.6 Laboratory Tests

Laboratory tests in patients with AAC are nonspecific. Leukocytosis is present in 70–85% of patients [68]. Abnormal liver tests include conjugated hyperbilirubinemia and a mild increase in serum alkaline phosphatase and serum aminotransferases [9].

Blood cultures should be acquired in all patients with suspected AAC to guide narrowing of empiric antibiotics (Table 3.1). However, the culture findings may be negative or inconclusive in late-stage disease [13], and bile culture results are negative in nearly 50% of patients with AAC, probably due to concurrent antibiotic therapy.

## 3.7 Imaging

Imaging in AAC is not specific enough to make a stand-alone diagnosis. Imaging findings must be integrated in the context of clinical presentation.

### 3.7.1 Ultrasonography

Ultrasonography in patients with suspected AAC is mandatory [56, 69]. Features suggestive of AAC are similar as the ones for ACC, but without gallstones [70]:

- Thick wall (≥3.5–4 mm) (with distended gallbladder of ≥5 cm longitudinally and no ascites)–the most reliable feature seen in patients with AAC but is not specific [71].
- Ultrasonographic Murphy's sign.
- Pericholecystic fluid (halo)/subserosal edema.
- Other signs: intramural gas, mucosal membrane, sludge, hydrops (distension ≥8 cm longitudinally or 5 cm transversely, with clear fluid).

The reported sensitivity of ultrasound for AAC ranges from 30% to 92% [71], while the specificity is 89–100% [3]. False-positive results may be due to hypoalbuminemia, ascites, sludge, non-shadowing stones, or cholesterolosis, which can mimic a thickened gallbladder wall.

### 3.7.2 Computed Tomography

When diagnosis is uncertain at ultrasound, contrast-enhanced abdominal computed tomography (CT) scan is recommended to confirm AAC and/or to rule out other causes for acute abdominal pain.

CT scan findings in AAC include gallbladder wall thickening (>3 mm), intramural gas, lack of gallbladder wall enhancement, subserosal and/or pericholecystic edema, pericholecystic fluid, mucosal sloughing, hyperdense bile (sludge), and/or gallbladder distention (>5 cm) [71] (Figs. 3.1, 3.2, and 3.3). Of these findings, gas in the gallbladder wall or lumen and pericholecystic edema have the highest specificity for AAC (99, 95, and 92%, respectively), but with poor sensitivity (11, 38, and 22%, respectively). The accuracy of CT scan appears to be like that seen with ultrasonography [72].

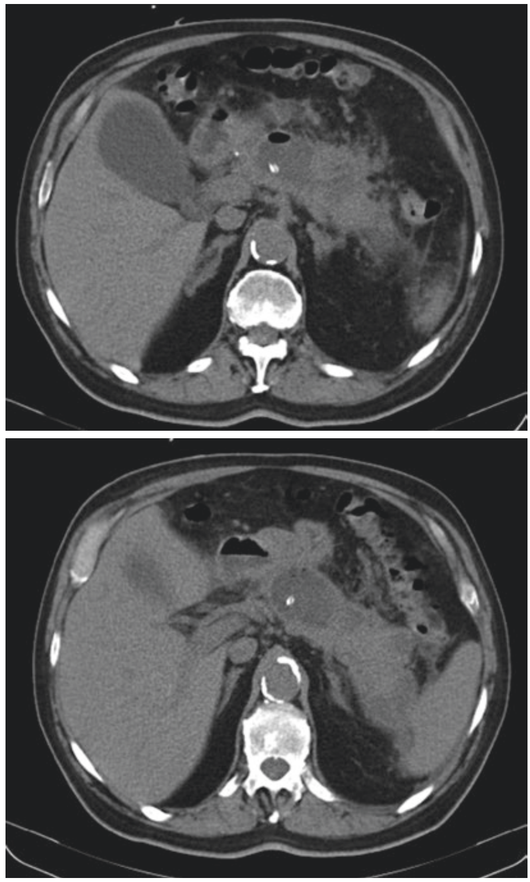

**Fig. 3.1** Control CT after percutaneous drainage of an infected pancreatic pseudocyst due to recent episode of acute alcoholic pancreatitis, in a 69-year old patient, with multiple comorbidities (obesity, third degree hypertension, dyslipidemia, hepatic steatosis, acute on chronic kidney condition stage G3a)

### 3.7.3 Cholescintigraphy

In stable patients with unclear diagnosis at ultrasonography and abdominal CT scan, a hepatic technetium 99 m Tc iminodiacetic acid (HIDA) scan is recommended [73]. As cholescintigraphy (HIDA scan) takes hours to perform, it is not recommended in critically ill patients in whom a delay in therapy can be potentially fatal; other arguments for not recommending it in this setting are the frequent false-negative and false-positive results (due to fasting, liver disease, or total parenteral nutrition) [74].

Failure to opacify the gallbladder at 1 h is considered positive for AAC. Leakage into the pericholecystic space indicates gallbladder perforation. The sensitivity of cholescintigraphy for AAC is 67–100% [74, 75], while the specificity is 58–88% [75].

Cholescintigraphy associated with intravenous morphine administration (0.05 mg/kg) has led to a reappraisal of HIDA imaging for AAC [75, 76], especially when ultrasound is nondiagnostic, increasing the diagnostic accuracy to 95% [75, 77]. AAC is diagnosed if the gallbladder is not visualized in 30 min after morphine injection.

False-negative results are rare occurring in certain conditions, such as cystic duct patency despite a diseased gallbladder, bowel loop simulation of the gallbladder, bile leak from gallblad-

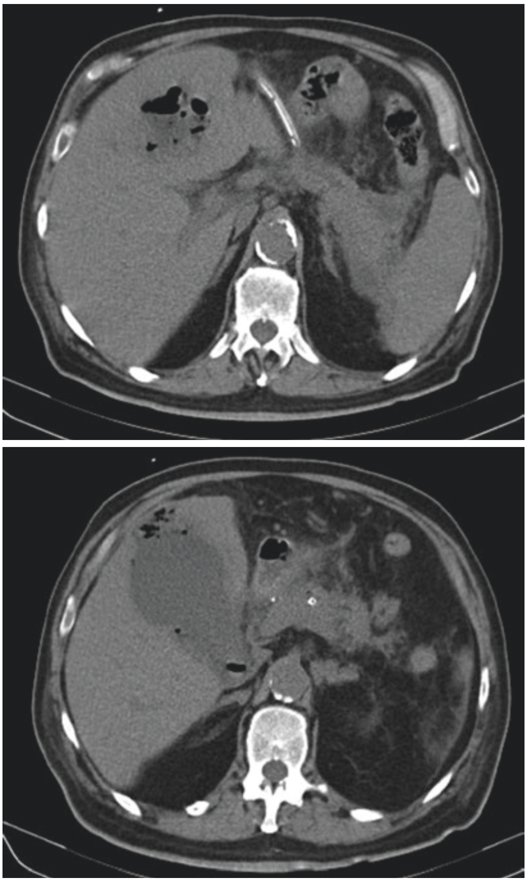

**Fig. 3.2** Same patient as in Fig. 3.1: CT at 3 weeks showing gallbladder with significant distension (115/80 mm), with thickened, irregular walls, nonhomogenous mixed fluid, para-fluid and multiple air blob contents, associated with significant densification of the adjacent fat structures, with inflammatory infectious aspect; continuity solution present at the level of the gallbladder fundic area, with intrahepatic penetration in the fourth liver segment, with gaseous, fluid, and parafluid accumulation at this level, approximately 50/45 mm in size axially, without biliary lithiasis—acute acalculous cholecystitis with in-hospital onset, in a critically ill patient, with pericholecystic liver abscess

der perforation, and tracer activity in the kidneys simulating the gallbladder [78]. False-positive results may occur in several conditions, such as fasting, total parenteral nutrition, severe illness, severe hepatocellular disease, hyperbilirubinemia, rapid biliary to bowel transit, biliary sphincterotomy, and/or prior cholecystectomy. Other

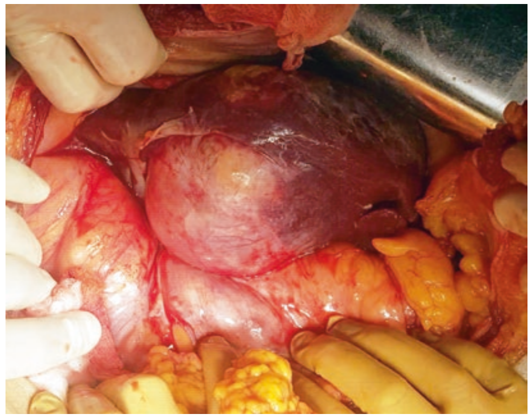

**Fig. 3.3** Same patient as in Figs. 3.1 and 3.2: Intraoperative aspect of acalculous cholecystitis with pericholecystic liver abscess (superficialized on the diaphragmatic surface of segments 4–5), for which subtotal cholecystectomy, liver abscess evacuation, and multiple drainage was performed. The patient died in POD 10 due to recurrent acute pancreatitis and multiple peritoneal abscesses, despite ICU aggressive treatment and surgical reintervention

agents (diisopropyl and m-bromothymethyl iminodiacetic acid) used in cholescintigraphy have generally overcome the limitations of morphine cholescintigraphy.

### 3.7.4 Laparoscopy

Laparoscopy is recommended when the diagnosis of AAC is in question or if percutaneous cholecystostomy has failed to improve the patient's general status [79]. Bedside laparoscopy has been used with certain success for both diagnosis and therapy of AAC, but initial enthusiasm has diminished due to the bulky equipment that has to be brought to the ICU bedside. Nowadays, due to advances in intensive care, most patients will tolerate the transport to the operating room. For severe local forms of AAC, when complete laparoscopic cholecystectomy is not possible in a safe and expedient manner, a laparoscopic damage control procedure such as cholecystostomy or partial cholecystectomy may be performed to treat the patient's condition while minimizing the iatrogenic aggression.

## 3.8 Diagnosis

### 3.8.1 Positive Diagnosis

AAC remains difficult to diagnose mainly due to complicated clinical settings [14], the low prevalence, and the complexities to distinguish it from ACC [37].

The diagnosis of AAC is based upon a series of symptoms and clinical signs (e.g., critically ill patients with sepsis without a clear cause or jaundice) correlated with imaging findings that support such diagnosis, and the exclusion of other diagnoses. Imaging in AAC is not specific enough to make the diagnosis alone and must be interpreted in the clinical context. AAC is often diagnosed based on the following:

- Fever, abdominal pain, leukocytosis, and/or elevated liver tests.
- Risk factors for AAC (Table 3.1).
- Imaging features suggesting AAC.
- No evidence of other conditions that explain the clinical and imaging findings.

After diagnosis, imaging has a monitoring role of the development of AAC during medical and interventional treatment. Sometimes, gallstones are discovered by imaging late, during nonsurgical treatment, converting the diagnosis from AAC to ACC, case in which cholecystectomy becomes mandatory (Fig. 3.4).

### 3.8.2 Differential Diagnosis

The differential diagnosis of AAC includes other causes of sepsis (e.g., pneumonia, urinary tract infection), right upper quadrant pain, and/or jaundice. These include:

- Acute calculous cholecystitis.
- Noninfectious gallbladder hydrops (Fig. 3.5).
- Noninfectious thick gallbladder wall.

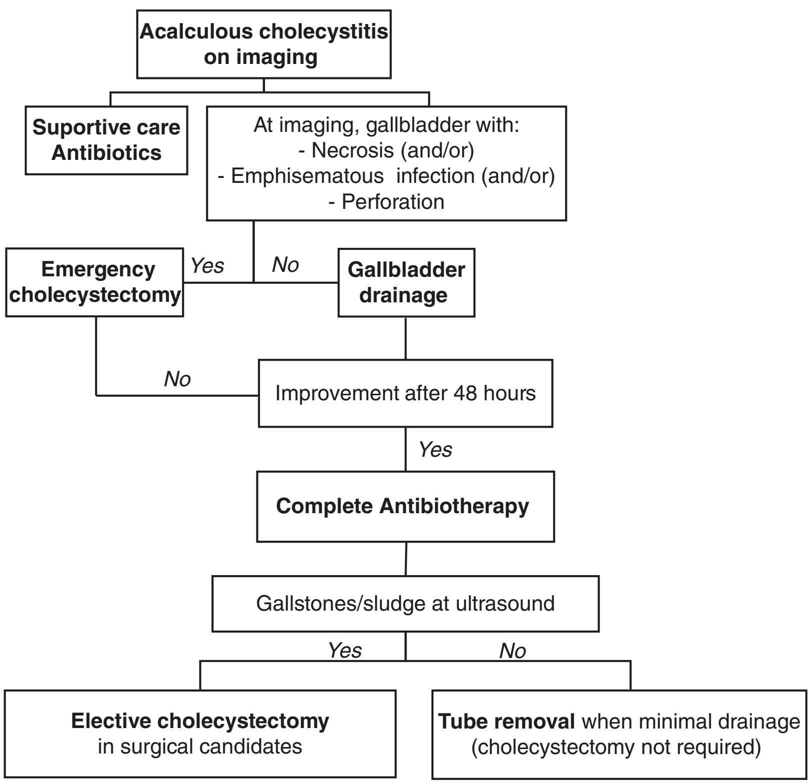


**Fig. 3.4** Approach to the management of acalculous cholecystitis

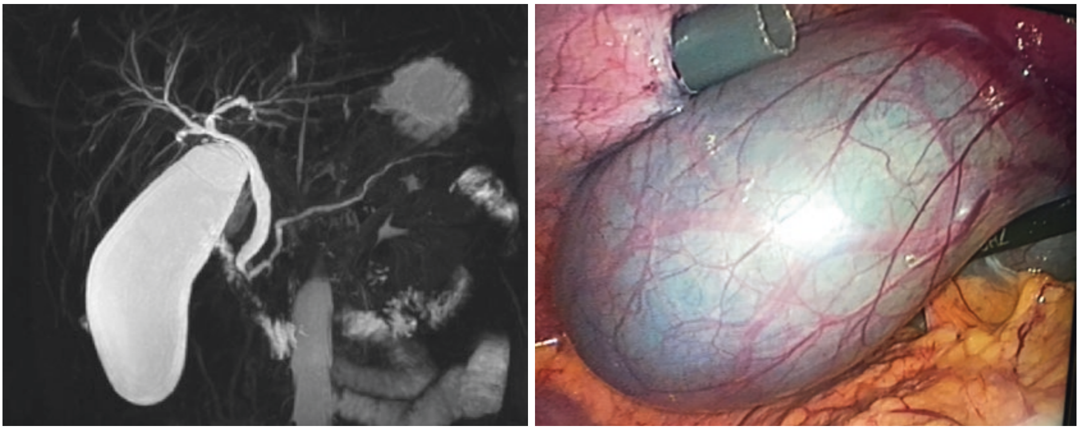

**Fig. 3.5** Noninfectious gallbladder hydrops (13 cm) due to stenosis of the terminal common bile duct induced by autoimmune pancreatitis (MRI imaging and intraoperative aspect during laparoscopic cholecystectomy) in a 23-year-old female patient, with Crohn's disease, autoimmune pancreatitis, type 1 ANA autoimmune hepatitis, autoimmune thyroiditis. Surgery consisted in laparoscopic cholecystectomy, with favorable outcome

– Acute pancreatitis.
– Hepatic or subphrenic abscess.
– Right-sided pyelonephritis.
– Right-sided pneumonia.
– Other causes for right upper quadrant pain.
– Other causes for jaundice.
– Other causes for sepsis and abdominal pain.

These conditions can be ruled out by clinical examination, laboratory tests, and imaging also performed for AAC diagnosis. Laboratory evaluation should include a complete blood count, electrolytes, liver tests, and pancreatic enzymes. In addition, a urine analysis to exclude urosepsis, and a chest X-ray or CT scan to exclude pneumonia.

### 3.8.3 Complications

Because of the potential obscurity of the diagnosis, the underlying illnesses of the affected patients, and the potentially rapid progression of the disease to emphysematous and gangrenous cholecystitis, and gallbladder perforation, complications associated with this condition are frequent and usually severe [53, 69]. Gallbladder necrosis, gangrene, and perforation are frequently present at the time of diagnosis, especially in the critically ill patients, being associated with poor outcome [53, 69]. The incidence of gallbladder gangrene is higher in the AAC than in ACC (31% vs 5%, respectively) [80]. Gallbladder gangrene occurs in approximately 50% of patients with AAC, commonly leading to gallbladder perforation [71]. Particularly, emphysematous cholecystitis increases the risk for perforation. Perforation occurs in approximately 10% of patients with AAC [7, 35] that may result in abscess formation, free perforation with generalized peritonitis or cholecystoenteric fistula. When gallbladder gangrene occurs without perforation, the common complications are acute pancreatitis, obstruction of the main bile duct, and colonic perforation.

The incidence of cerebrovascular accidents is significantly higher in patients with acute AAC than in those with ACC (15% vs 6%) [80].

### 3.8.4 Mortality

AAC is associated with a high mortality rate, which depends on comorbidities and the swiftness of diagnosis. The cause of death in most patients with AAC is multiorgan failure due to sepsis [81]. The mortality rate is related to the initial clinical severity and a high prevalence of gangrene (approximately 50%) and perforation (approximately 10%) [37], but always greater than 1% reported in gallstone cholecystitis [70].

With treatment, the overall mortality rate is high (30%) [7, 71, 82], but it increases to up to 75% if diagnosis and treatment are delayed [83]. The mortality rate in critically ill patients is very high, up to 90%, while in outpatient cases may be as low as 10% [71, 84].

## 3.9 Conclusion

AAC is very difficult to diagnose and should be screened in all critically ill or injured patients with sepsis, especially in cases where the cause of sepsis is not clear, in case of hypoperfusion, onset of jaundice, and/or postoperative setting. Ultrasound is the main diagnostic tool, being repeatable, noninvasive, cost-effective, and bedside available. The diagnosis must be prompt, otherwise mortality increases significantly.

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# 4 Guidelines for the Management of Acute Cholecystitis

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## 4.1 Introduction

Despite being a common disease, there are significant controversies regarding the diagnosis and management of acute calculous cholecystitis (ACC). The 2007 and 2013 Tokyo guidelines (TG) attempted to establish objective parameters for the diagnosis of ACC [1, 2]. While the TG have certainly improved the understanding of ACC, some criticisms have followed [3, 4]. There continue to be debates regarding the diagnostic value of single ultrasound (US) signs, as well as of laboratory tests. Historically, with regard to the treatment of ACC, the main controversy surrounded timing of surgery. The need for surgery versus conservative management has been less investigated, particularly in high-surgical-risk patients. A thorough discussion of the limitations of the Tokyo Guidelines goes beyond the aim of this chapter (see Chap. 5), but these limitations were the impetus for the World Society of Emergency Surgery (WSES) to convene a consensus conference. This consensus conference led to the creation of the 2016 WSES guidelines on ACC [5]. After the creation of these guidelines, the MICOL study [6] revealed the high incidence of gallstones and ACC in the elderly population and highlighted unique characteristics of this patient population. Because of these results, the WSES and SICG (Italian Society of Geriatric Surgery) joined forces to convene another consensus conference focusing on acute cholecystitis in the elderly population. Their efforts led to the creation of the 2017 WSES/SICG guidelines on ACC in the elderly population [7]. The aim of this chapter is to combine and briefly summarize the WSES guidelines on ACC and to provide a quick and easy-to-use tool for physicians treating this challenging disease.

## 4.2 Materials and Methods

The Scientific Board of the WSES organized the consensus conference on ACC in order to develop the WSES Guidelines on this topic. It is important to note that these guidelines should serve as an adjunct to clinical decision-making but do not replace clinical judgment in the context of an individual patient. The WSES President appointed four members to a Scientific Secretariat, eight members to an Organization Committee, and eight members to a Scientific Committee. Eight relevant key questions regarding diagnosis and treatment of ACC were developed to thoroughly analyze the topic. Before the

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consensus conference, a number of statements were developed for each of the main questions, along with the Level of Evidence (LoE) and the Grade of Recommendation (GoR) for each statement. The consensus conference on ACC was held in Jerusalem, Israel, on July 6th, 2015 during the 3rd World Congress of the WSES. Each statement was then voted upon by the audience, and comments on each statement were collected. Before the second part of the consensus conference, the president and representatives from the Organization Committee, Scientific Committee, and Scientific Secretariat modified the statements according to the findings of the first session. The revised statements were then presented again to the audience. During this process, a comprehensive algorithm for the treatment of ACC was developed based on the results of the first session of the consensus conference and voted upon for definitive approval.

The eight topics investigated during the first consensus conference were:

1. Diagnosis of ACC: Investigations.
2. Treatment of ACC: Best options.
3. Antibiotic therapy for ACC.
4. Patient selection for surgery: Risk stratification, i.e., definition of high-risk patients.
5. Timing for surgery for ACC.
6. Type of surgery for ACC.
7. Associated common bile duct stone: Suspicion and diagnosis at the presentation.
8. Alternative treatments for high-risk patients.

The methods used to inform the 2017 WSES/SICG guidelines mirror those used for the 2016 WSES guidelines. However, the consensus conference was held in 2017 during the 30th annual congress of SICG. The aim of the consensus conference was to investigate age-related factors that could influence diagnosis and management of ACC in people ages 65 and older.

Although the age cutoff of 65 was chosen arbitrarily, it is important to note that the definition of “old age” is a composite of various factors including chronological age, social factors, economic and cultural factors, and functional status. Six relevant key questions regarding diagnosis and treatment of ACC in elderly people were developed to thoroughly analyze the topic. The 2016 WSES Guidelines on ACC were used as the main point of reference.

The six topics investigated during the second consensus conference were:

1. Diagnosis: Which test is most useful in the elderly?
2. How to weigh pro and cons of surgery in elderly patients with ACC?
3. What is the most appropriate timing and the most appropriate surgical technique for elderly?
4. Alternative treatments in case of reduced benefit from surgery in elderly: Is there a role for percutaneous cholecystostomy?
5. Associated biliary tree stones: What test for suspicion, what treatment, when to treat it?
6. Antibiotic: What schedule for treatment?

## 4.3 Discussion

The results of the two consensus conferences and the associated guidelines are summarized in Tables 4.1 and 4.2.

### 4.3.1 Diagnosis

Although ACC is a common disease encountered in the Emergency Department, its diagnosis remains a major challenge. Evidence of an inflamed gallbladder containing stones is the diagnostic cornerstone. The diagnosis of ACC is based on clinical findings, laboratory data, and imaging studies. The diagnostic performance of an abdominal ultrasound (AUS) in the diagnosis of inflammation of the gallbladder is not as good as its performance in the diagnosis of gallstones, as indicated in a recent meta-analysis [8]. However, its widespread availability, lack of invasiveness, lack of exposure to ionizing radiation, and a short duration of examination make it the first-choice imaging investigation for the diagnosis of ACC. The same meta-analysis by Kieiwiet et al. [8] included studies on CT, MRI, and HIDA

**Table 4.1** 2016 WSES Guidelines, STATEMENTS

| | |
|---|---|
| *Diagnosis: Investigation* | |
| 1.1 | There is no single clinical or laboratory finding with sufficient diagnostic accuracy to establish or exclude acute cholecystitis (LoE 2 GoR B). Combination of detailed history, complete clinical examination, and laboratory tests may strongly support the diagnosis of ACC (LoE 4 GoR C) |
| 1.2 | Abdominal ultrasound (AUS) is the preferred initial imaging technique for patients who are clinically suspected to have ACC because of its lower cost, better availability, lack of invasiveness, and high accuracy for gallbladder stones (LoE 2 GoR B) |
| 1.3 | AUS exploration is a fairly reliable investigation method but its sensitivity and specificity for diagnosing ACC are relatively low according to the adopted AUS criteria (LoE 3 GoRC) |
| 1.4 | Evidence on the diagnostic accuracy of computed tomography (CT) is scarce. While diagnostic accuracy of magnetic resonance imaging (MRI) might be comparable to that of AUS, insufficient data are available to support it. Hepatobiliary iminodiacetic acid scan (HIDA scan) has the highest sensitivity and specificity for acute cholecystitis, although its scarce availability, long time required to perform the test, and exposure to ionizing radiation limit its use (LoE 2 GoRB) |
| 1.5 | Combining clinical, laboratory, and imaging investigations is recommended, although the best combination is not yet known (LoE 4 GoRC) |
| *Treatment: Best options* | |
| 2.1 | There is no role for gallstones dissolution, drugs, or extracorporeal shock wave lithotripsy (ESWL) or a combination in the setting of ACC (LoE 2 GoR B) |
| 2.2 | Since there are no reports on surgical gallstone removal in the setting of ACC, surgery in the form of cholecystectomy remains the main option (LoE 4 GoR C) |
| 2.3 | Surgery is superior to observation of ACC in the clinical outcome and shows some cost-effectiveness advantages due to the gallstone-related complications and to the high rate of readmission and surgery in the observation group (LoE 3 GoR C) |
| 2.4 | Antibiotics should be suggested as supportive care; they are effective in treating the first episode of ACC but a high rate of relapse can be expected. Surgery is more effective than antibiotics alone in the treatment of ACC (LoE 2 GoR C) |
| 2.5 | Cholecystectomy is the gold standard for treatment of ACC (LoE 3 GoR C) |
| 2.6 | If surgery is not available, medications such as antibiotics and analgesic should be prescribed, and the patients should be referred to a surgical center (depending upon the general condition) due to the high rate of gallstone-related events (LoE 5 GoR D) |
| *Antibiotic therapy* | |
| 3.1 | Patients with uncomplicated cholecystitis can be treated without postoperative antibiotics when the focus of infection is controlled by cholecystectomy (LoE 1 GoR B) |
| 3.2 | In complicated acute cholecystitis, the antimicrobial regimens depend on presumed pathogens involved and risk factors for major resistance patterns (LoE 3 GoR B) |
| 3.3 | The results of microbiological analysis are helpful in designing targeted therapeutic strategies for individual patients to customize antibiotic treatment and ensure adequate antimicrobial coverage in patients with complicated cholecystitis and at high risk for antimicrobial resistance (LoE 3 GoR C) |
| *Patient selection for surgery: Risk stratification* | |
| 4.1 | Patient's age above 80 in ACC is a risk factor for worse clinical behavior, morbidity, and mortality (LoE 3 GoR B) |
| 4.2 | The coexistence of diabetes mellitus does not contraindicate urgent surgery but must be reconsidered as a part of the overall patient comorbidity (LoE 3 GoR C) |
| 4.3 | Currently, there is no evidence of any scores in identifying patient's risk in surgery for ACC. ASA, POSSUM, and APACHE II are correlated to surgical risk in patients with gallbladder perforation, higher accuracy being for APACHE II. However, APACHE II is built to predict morbidity and mortality in the patients admitted to ICU; its use as a preoperative score should be considered as an extension usage from the original concept. (LoE 4 GoR C) |
| *Timing for surgery* | |
| 5.1 | Early laparoscopic cholecystectomy is preferable to delayed laparoscopic cholecystectomy in patients with ACC as long as it is completed within 10 days of onset of symptoms (LoE 1 GoR A) |

(continued)

**Table 4.1** (continued)

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|---|---|
| 5.2 | Laparoscopic cholecystectomy should not be offered for patients beyond 10 days from the onset of symptoms unless symptoms suggestive of worsening peritonitis or sepsis warrant an emergency surgical intervention. In people with more than 10 days of symptoms, delaying cholecystectomy for 45 days is better than immediate surgery (LoE 2 GoR B) |
| 5.3 | Early laparoscopic cholecystectomy should be performed as soon as possible but can be performed up to 10 days of onset of symptoms. (level 1 evidence; grade A recommendation). However, it should be noted that earlier surgery is associated with shorter hospital stay and fewer complications (LoE 2 GoR B) |
| *Type of surgery* | |
| 6.1 | In ACC, a laparoscopic approach should initially be attempted except in case of absolute anaesthesiology contraindications or septic shock (LoE 2 GoR B) |
| 6.2 | Laparoscopic cholecystectomy for ACC is safe, feasible, with a low complication rate, and associated with shortened hospital stay (LoE 1 GoR A) |
| 6.3 | Among high-risk patients, in those with child A and B cirrhosis, advanced age > 80, or pregnant women, laparoscopic cholecystectomy for ACC is feasible and safe (LoE 3 GoR C) |
| 6.4 | Laparoscopic or open subtotal cholecystectomy is a valid option for advanced inflammation, gangrenous gallbladder, or any setting of the “difficult gallbladder” where anatomy is difficult to recognize and main bile duct injuries are more likely (LoE 2 GoR A) |
| 6.5 | In case of local severe inflammation, adhesions, bleeding in Calot’s triangle, or suspected bile duct injury, conversion to open surgery should be strongly considered. (LoE 3 GoR B) |
| *Associated common bile duct stones* | |
| 7.1 | Elevation of liver biochemical enzymes and/or bilirubin levels is not sufficient to identify ACC patients with choledocholithiasis, and further diagnostic tests are needed (LoE 2 GoR B) |
| 7.2 | At AUS, the visualization of CBDS is a very strong predictor of choledocholithiasis. (LoE 5 GoR D). Indirect signs of stone presence such as increased diameter of common bile duct are not sufficient to identify ACC patients with choledocholithiasis, and further diagnostic tests are needed. (LoE 1 GoR A) |
| 7.3 | Liver biochemical tests, including ALT, AST bilirubin, ALP, gamma glutamyl transferase (GGT), AUS should be performed in all patients with ACC to assess the risk for CBS (LoE 2 GoR B) |
| 7.4 | Common bile duct stone risk should be stratified according to the proposed classification, modified from the American Society of Gastrointestinal Endoscopy and the Society of American Gastrointestinal Endoscopic Surgeon Guidelines (LoE 5 GoR D) |
| 7.5 | Patients with moderate risk for choledocholithiasis should undergo preoperative MRCP, EUS, intraoperative cholangiography, or laparoscopic ultrasound depending on the local expertise and availability. (LoE 1 GoR A) |
| 7.6 | Patients with high risk for choledocholithiasis should undergo preoperative ERCP, intraoperative cholangiography, laparoscopic ultrasound, depending on the local expertise and the availability of the technique. (LoE 1 GoR A) |
| 7.7 | CBDS could be removed preoperatively, intraoperatively, or postoperatively according to the local expertise and the availability of the technique (LoE 1 GoR A) |
| *Alternative treatments for high-risk patients* | |
| 8.1 | Gallbladder drainage, together with antibiotics, converts a septic cholecystitis into a nonseptic condition; however, the level of evidence is poor (LoE 4, GoR C) |
| 8.2 | Among standardized gallbladder drainage techniques percutaneous transhepatic gallbladder drainage (PTGBD) is generally recognized as the preferred technique due to the ease and the reduced costs (LoE 4, GoR C) |
| 8.3 | Percutaneous cholecystostomy could be considered as a possible alternative to surgery after the failure of conservative treatment in a small subset of patients unfit for emergency surgery due to their severe comorbidities (LoE 2 GoR B) |
| 8.4 | Delayed laparoscopic cholecystectomy could be offered to patients after reduction of operative and anesthesiology-related risks to reduce further hospitalization (LoE 5 GoR D) |

**Table 4.2** 2017 WSES/SICG Elderly Guidelines, STATEMENTS

| | |
|---|---|
| *Diagnosis* | |
| 1.1 | There is no single investigation with sufficient diagnostic power to establish or exclude acute cholecystitis without further testing even in elderly people (LoE 2 GoR B). Combination of symptoms, signs, and laboratory tests results may have better diagnostic accuracy in confirming the diagnosis of ACC (LoE 4 GoR D) |
| 1.2 | Abdominal ultrasound is the preferred initial imaging technique for elderly patients who are clinically suspected of having acute cholecystitis, in terms of lower costs, better availability, lack of invasiveness, and good accuracy for stones (LoE 3 GoR C) |
| 1.3 | Even in elderly patients, evidence on the diagnostic accuracy of CT are scarce and remain elusive while diagnostic accuracy of MRI might be comparable to that of abdominal ultrasound, but no sufficient data are provided to support this hypothesis. HIDA scan has the highest sensitivity and specificity for acute cholecystitis than other imaging modalities although its scarce availability, long time of execution, and exposure to ionizing radiations limit its use (LoE 3 GoR C) |
| 1.4 | Even in elderly patients, combining clinical, laboratory, and imaging investigations should be recommended, although the best combination is not yet known (LoE 5 GoR D) |
| 1.5 | No high-quality studies on specific diagnostic findings of acute cholecystitis in the elderly have been found; therefore, the stated recommendations of the WSES guidelines previously reported remain unchanged (LoE 4 GoR D) |
| *Surgical risk assessment and treatment* | |
| 2.1 | Old age (>65 years), by itself, does not represent a contraindication to cholecystectomy for ACC (LoE 3 GoR B) |
| 2.2 | Cholecystectomy is the preferred treatment for ACC even in elderly patients (LoE 3 GoR C) |
| 2.3 | The evaluation of the risk for elderly patient with ACC should include:<br>1. Mortality rate for conservative and surgical therapeutic options<br>2. Rate of gallstone-related disease relapse and the time to relapse<br>3. Age-related life expectancy<br>4. Consider patient frailty evaluation by the use of frailty scores<br>5. Consider estimation of specific risk (patient/type of surgery) by the use of surgical clinical scores (LoE 3 GoR C) |
| *Timing and surgical technique* | |
| 3.1 | In elderly patients with acute cholecystitis, laparoscopic approach should always be attempted at first except in the case of absolute anesthetic contraindications and septic shock (LoE 2 GoR B) |
| 3.2 | In elderly patients, laparoscopic cholecystectomy for acute cholecystitis is safe, feasible, with a low complication rate, and associated with shortened hospital stay (LoE 2 GoR B) |
| 3.3 | In elderly patients, laparoscopic or open subtotal cholecystectomy is a valid option for advanced inflammation, gangrenous gallbladder, and "difficult gallbladder" where anatomy is difficult to be recognized, and main bile duct injuries are highly probable (LoE 3 GoR C) |
| 3.4 | In elderly patients, conversion to open surgery may be predicted by fever, leucocytosis, elevated serum bilirubin, and extensive upper abdominal surgery. In case of local severe inflammation, adhesions, bleeding in the Calot's triangle, and suspect bile duct injury, conversion to open surgery should be considered (LoE 3 GoR C) |
| 3.5 | Even in elderly patients, early laparoscopic cholecystectomy should be performed as soon as possible but can be performed up to 10 days of onset of symptoms. However, it should be noted that earlier surgery is associated with shorter hospital stay and fewer complications (LoE 2 GoR B) |
| *Alternative treatments* | |
| 4.1 | Percutaneous cholecystostomy can be considered in the treatment of ACC patients (older than 65, with ASA III/IV, performance status 3 to 4, or septic shock) who are deemed unfit for surgery (LoE 2 GoR B) |
| 4.2 | If medical therapy failed, percutaneous cholecystostomy should be considered as a bridge to cholecystectomy in acutely ill (high-risk) elderly patients deemed unfit for surgery, in order to convert them in a moderate-risk patient, more suitable for surgery (LoE 3 GoR C) |
| 4.3 | As in the general population, even in elderly patients, percutaneous transhepatic cholecystostomy is the preferred method to perform percutaneous cholecystostomy (LoE 4 GoR D) |

(continued)

**Table 4.2** (continued)

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| 4.4 | As in the general population, even in elderly patients, percutaneous cholecystostomy catheter should be removed between 4 and 6 weeks after placement, if a cholangiogram performed 2–3 weeks after percutaneous cholecystostomy demonstrated biliary tree patency (LoE 3 GoR C) |
| *Associated common bile duct stones* | |
| 5.1 | Even in elderly patients, elevation of liver biochemical enzymes and/or bilirubin levels is not sufficient to identify ACC patients with choledocholithiasis, and further diagnostic tests are needed. (LoE 3 GoR C) |
| 5.2 | Even in elderly patients, the visualization of common bile duct stones on abdominal ultrasound is a very strong predictor of choledocholithiasis (LoE 5 GoR D). Even in elderly patients, indirect signs of stone presence such as increased diameter of common bile duct are not sufficient to identify ACC patients with choledocholithiasis, and further diagnostic tests are needed. (LoE 2 GoR B) |
| 5.3 | Liver biochemical tests, including ALT, AST, bilirubin, ALP, GGT, and abdominal ultrasound should be performed in all patients with ACC to assess the risk for common bile duct stones. (LoE 3 GoR C). Even in elderly patients, common bile duct stone risk should be stratified according to the proposed classification, modified from the American Society of Gastrointestinal Endoscopy and the Society of American Gastrointestinal Endoscopic Surgeon Guidelines (LoE 5 GoR D) |
| 5.4 | Even in elderly patients with moderate risk for choledocholithiasis preoperative magnetic resonance cholangiopancreatography (MRCP), endoscopic US, intraoperative cholangiography, or laparoscopic ultrasound should be performed depending on the local expertise and availability (LoE 2 GoR B) |
| 5.5 | Elderly patients with high risk for choledocholithiasis should undergo preoperative ERCP, intraoperative cholangiography, or laparoscopic ultrasound, depending on the local expertise and the availability of the technique (LoE 2 GoR B) |
| 5.6 | Even in elderly patients, common bile duct stones could be removed preoperatively, intraoperatively, or postoperatively according to the local expertise and the availability of the technique (LoE 2 GoR B) |
| *Antibiotic therapy* | |
| 6.1 | Elderly patients with uncomplicated cholecystitis can be treated without postoperative antibiotics when the focus of infection is controlled by cholecystectomy (LoE 2 GoR C) |
| 6.2 | In elderly patients with complicated acute cholecystitis, antibiotic regimens with broad spectrum are recommended as adequate empiric therapy significantly affects outcomes in critical elderly patients. The principles of empiric antibiotic therapy should be guided by most frequently isolated bacteria taking into consideration antibiotic resistance and the clinical condition of the patient (LoE 2 GoR B) |
| 6.3 | The results of microbiological analysis are helpful in designing targeted therapeutic strategies for individual patients with healthcare infections to customize antibiotic treatments and ensure adequate antimicrobial coverage (LoE 5 GoR D) |

in addition to those on AUS. In a head-to-head comparison, the diagnostic accuracy of MRI was comparable with that of AUS. Data on the diagnostic accuracy of CT is limited, and CT exposes patients to ionizing radiation. CT is therefore usually indicated when sonography is nondiagnostic or patients have confusing signs and symptoms [9]. Although radiological investigation by HIDA may be required to reach diagnostic certainty, its utility is limited by its lack of availability, long examination duration, and inability to image the biliary tract. Furthermore, since symptomatic gallbladder stones are, in any case, an indication for laparoscopic cholecystectomy, the AUS diagnostic uncertainty may not be relevant in healthy patients and invasive radiological investigation, such as HIDA, should therefore be applied only in high-risk patients. To further complicate the diagnostic process, age-related changes involving pain perception [10, 11], biliary tract physiology [12], and stress response to tissue injury [13, 14] may modify the clinical picture of ACC occurring in an elderly patient. A full clinical examination should be performed and recorded and this should be combined with laboratory tests for inflammation and AUS. When there are uncertain findings on AUS imaging with clinical suspicion of ACC, there is no definitive evidence in favor of using a high cost although highly accurate investigation (HIDA or MRI) or of treating the patient empirically as if he or she had ACC. It is important to keep in mind that aging is a risk factor for gangrenous cholecystitis and that a higher rate of severe cholecystitis has been reported in the elderly patient group [15].

### 4.3.2 Surgical Therapy and Risk Stratification

ACC is a heterogeneous condition and the severity of inflammation and its life-threatening potential are strongly determined by the overall status of the patient. Regarding ACC treatment, different gallstone-removal techniques besides cholecystectomy have not been tested in the acute setting and there is a paucity of evidence about this technique. We found one prospective randomized study by Schmidt et al. (2016) comparing observation to surgery after ACC [16]. The sample size was 33 patients assigned to observation versus 31 assigned to surgery. After an average follow-up period of 14 years, 33% (11 patients) in the observation group experienced relapse of gallstone disease and all required surgery. On the basis of Schmidt et al.'s findings and a RCT on symptomatic but uncomplicated gallstone disease [17], Brazzelli et al. produced a clinical and cost-effectiveness analysis, comparing surgery to observation, using a UK-based economic model [18, 19]. They found that patients randomized to observation experienced a higher rate of gallstone-related complications (14% versus 2%) when compared to surgical group. These complications occurred more frequently in patients with ACC than in those with biliary colic only. Nowadays, laparoscopy is the gold standard for ACC surgery. Laparoscopic approach is safer than open approach for ACC: the morbidity and mortality, in the case of laparoscopic procedure are 10% and 1%, respectively, compared to 25% and 2% for open procedure [20]. Coccolini and colleagues in 2015 published a systematic review and meta-analysis with the focus of comparing open and laparoscopic cholecystectomy for ACC, and the morbidity and mortality analysis favors the use of the laparoscopic procedure [21]. Laparoscopic or open subtotal cholecystectomy is a valid option for advanced inflammation, gangrenous gallbladder, or any setting of a "difficult gallbladder" where the anatomy is difficult to recognize and main bile duct injuries are more likely. A recent systematic review with meta-analysis by Elshaer et al. [22] reported that subtotal cholecystectomy was performed using the laparoscopic (72.9%), open (19%), and laparoscopic converted to open (8%) techniques. They concluded that subtotal cholecystectomy is an important tool in the difficult cholecystectomy and achieves morbidity rates comparable to those reported for total cholecystectomy in simple cases. An alternative surgical strategy is the fundus-first approach, although the risk of lesions in this approach must be kept in mind [23, 24]. According to Giger et al., extensive inflammation, adhesions, and consequent increased exudate can make laparoscopic dissection of Calot's triangle and recognition of the biliary anatomy hazardous and difficult. Therefore, conversion to open surgery is strongly recommended to ensure patient safety in such difficult conditions [25]. In conclusion, gangrenous gallbladder, obscure anatomy, bleeding, bile duct injuries, adhesions, and previous upper abdominal surgery represent clinical conditions for which conversion to open cholecystectomy should be strongly considered. However, the recommendations regarding surgical treatment of ACC are limited to patients who may be good candidates for urgent surgery. Unfortunately, gray areas remain in cases of patients unfit for urgent surgery or for laparoscopic surgery due to general comorbid conditions. Furthermore, older patients require further considerations when suggesting surgery for ACC. However, a large retrospective cohort study including 29,918 patients with ACC demonstrated that the mortality rate of elderly patients (mean age 77.7 years) is significantly lower in those undergoing surgery during the same admission compared to those discharged home without receiving surgery during the initial admission [20]. The scientific evidence coming from the literature allows us to consider cholecystectomy during the initial admission as the preferred treatment for all patients with ACC, including the elderly. To achieve this, elderly patients require a more detailed and rapid evaluation compared to the general population to take into account the higher susceptibility of elderly patients. A systematic review of retrospective studies was performed in 2017 and focused its attention on the safety of early cholecystectomy in 592 elderly patients (mean age 81 years) with a high surgical risk (American Society of Anesthesiologist (ASA) status ≥3 in 44% of the included patients); the authors concluded that early cholecystectomy is feasible because the overall mortality was 3% and the morbidity was 23%, which was similar to that in the younger population (1% and 15%, respectively) [26]. In the setting of ACC and old age, a single "rule" for all patients cannot be applied, and research is necessary to stratify the surgical risk. ASA, P-POSSUM, and APACHE II showed the best correlation with surgical risk, but there is no validated way of stratifying risk in elderly patients, even though age is one of the factors considered for calculation of P-POSSUM and APACHE II scores. Frailty scoring systems may help in stratifying the risk.

### 4.3.3 Timing for Surgery

Several RCTs have investigated early laparoscopic cholecystectomy versus delayed laparoscopic cholecystectomy. Different trials have used varying definitions for early and delayed laparoscopic cholecystectomies. In general, early laparoscopic cholecystectomy has been defined either as being performed in patients with acute cholecystitis with symptoms for less than 72 h or as patients with acute cholecystitis with symptoms for less than 7 days but within 4–6 days of diagnosis, which roughly translates to 10 days from onset of symptoms. Although the historical rule of 72 h to perform cholecystectomy for ACC is no longer mandatory, surgery performed as soon as possible is associated with a better outcome [27–30]. Moreover, the expected reduction in reserve capacity in older patients should prompt rapid treatment if possible. One trial compared early laparoscopic cholecystectomy versus delayed laparoscopic cholecystectomy performed between 7 days and 45 days after initial diagnosis [28]. This trial demonstrated that the morbidity was higher, and the length of hospital stay was 5 days longer in the delayed laparoscopic cholecystectomy group compared to the early laparoscopic cholecystectomy group. Evidence from a large database review including approximately 95,000 patients with ACC demonstrated that patients who had surgery within 2 days of admission had fewer complications than those who underwent surgery between 2 and 5 days after admission, and those who had surgery between 6 days and 10 days of presentation. There was no significant difference in the groups between conversion to open surgery [30].

### 4.3.4 Antibiotic Therapy

Alongside surgical treatment, therapy with appropriate antibiotic agents is an important component in the management of patients with ACC [31, 32]. Antibiotics are always recommended in complicated cholecystitis and in delayed management of uncomplicated cholecystitis. In a recently published prospective RCT [33], a total of 414 patients treated at 17 French medical centers for grade I or II ACC and who received 2 g of amoxicillin plus clavulanic acid three times a day and once at the time of surgery were randomized after surgery. Patients were randomized to either no antibiotics after surgery or continuation with the preoperative antibiotic regimen three times daily for 5 days. Among patients with mild ACC who received preoperative and intraoperative antibiotics, lack of postoperative treatment with amoxicillin plus clavulanic acid did not result in a greater incidence of postoperative infections. The principles of empiric antibiotic treatment should be defined according to the most frequently isolated microbes, always taking into consideration the local trend of antibiotic resistance. Organisms most often isolated in biliary infections are gram-negative aerobes, *Escherichia coli*, and Klebsiella pneumonia and anaerobes, especially *Bacteroides fragilis* [34, 35]. Healthcare-related infections are commonly caused by more resistant strains. For these infections, broader spectrum regimens are recommended because adequate empiric therapy appears to be a crucial factor affecting postoperative complications and mortality rates, especially in critically ill patients [36]. The efficacy of antibiotics in the treatment of biliary infections depends on the concentration of the antibiotic in the biliary tract, which may be limited in patients with obstructed bile ducts [37]. The choice of antibiotic regimen may be problematic in the management of critically ill patients with ACC. In patients with severe sepsis or septic shock of abdominal origin, early, appropriate empirical antibiotic therapy has a significant impact on outcomes [38]. Recent international guidelines for the management of severe sepsis and septic shock (Surviving Sepsis Campaign) recommend intravenous antibiotics within the first hour after severe sepsis and septic shock are recognized, use of broad-spectrum agents with good penetration into the presumed site of infection, and reassessment of the antimicrobial regimen daily to optimize efficacy, prevent resistance, avoid toxicity, and minimize costs [39]. Identifying the causative organism(s) is an essential step in the management of ACC, especially in patients with infections at high risk for antibiotic resistance such as healthcare-associated infections. Management of antibiotics in the elderly patient is often a major challenge. Advancing age is accompanied by changes in the pharmacokinetics and pharmacodynamics of antibiotics that often can be exacerbated by renal effects of coexisting diseases. Moreover, elderly patients in institutions, such as nursing homes or geriatric hospitals, pose a particular challenge. Frailty combined with suboptimal hygiene (e.g., often the case in patients with dementia) can promote rapid dissemination of multidrug-resistant organisms (MDROs).

### 4.3.5 Associated Common Bile Duct Stones

Choledocholithiasis, i.e., the presence of common bile duct stones (CBDS), is reported to occur in 10–20% of cholelithiasis cases, with a lower incidence in ACC ranging from 5% to 15% [40–42]. Investigation for CBDS requires time and can delay surgical intervention. Due to the relatively low incidence of CBDS during ACC, the challenge is to identify patients with a high likelihood of CBDS who would benefit from further diagnostic tests and eventual stone removal. Historically, liver function tests have great utility in determining the presence of CBDS. However, the majority of published studies are not in patients with ACC and also include asymptomatic cholelithiasis. In fact, in ACC, liver function tests may be altered due to the acute inflammatory process of the gallbladder and the biliary tree and up to 15–50% of patients with ACC show elevation in liver enzymes without choledocholithiasis. Chang et al. showed that 51% and 41% of ACC patients without choledocholithiasis had elevated ALT and AST, respectively. However, increased bilirubin levels with leukocytosis may predict gangrenous cholecystitis [43]. The diagnostic accuracy increases for cholestasis tests such as serum bilirubin with the duration and the severity of obstruction. Specificity of serum bilirubin level for CBDS was 60% with a cutoff level of 1.7 mg/dL and 75% with a cutoff level of 4 mg/dL [44]. AUS, the preferred imaging technique to diagnose ACC, can simultaneously visualize the gallbladder and common bile duct. Although visualization of CBDS is a very strong predictor of choledocholithiasis, a retrospective analysis by Boys et al. concluded that AUS-identified common bile duct diameter is not sufficient to identify patients at significant risk for CBDS [45]. Several predictive scores of CBDS have been proposed and validated but none are specific for ACC. The implementation of these predictive scores in clinical practice is poor. The American Society of Gastrointestinal Endoscopy and the Society of American of Gastrointestinal Endoscopic Surgeons combined the various published validated clinical scores and proposed a risk stratification of CBDS into three different classes: low risk (<10%), moderate (10 to 50%), and high risk (>50%), based on the presence of predictive factors for having CBDS [46]. The ASGE guidelines seem to be the best available tool for the diagnosis and the management of

CBDS during ACC. However, according to this classification, high-risk patients have a >50% probability of having CBDS; this means that up to 49% of patients that undergo ERCP may have no CBDS. For this reason, we prefer a more cautious approach; only patients with evidence of CBDS on AUS should be considered at high risk of CBDS and should directly undergo diagnostic and therapeutic ERCP. Two preoperative imaging techniques are available for the detection of CBDS, MRCP, and EUS. Although these diagnostic tools could delay ACC treatment, they could also exclude the presence of CBDS with high diagnostic accuracy, thereby avoiding further invasive procedures such ERCP or intraoperative cholangiography and their complications. ERCP has both a diagnostic and therapeutic role in the management of choledocholithiasis but is an invasive procedure with severe potential complications. On the other hand, intraoperative cholangiography significantly increases the length of surgery [47] and requires dedicated staff in the operating room that may not be available, especially in the acute setting. Furthermore, intraoperative evidence of CBDS, either via cholangiography or laparoscopic ultrasound, leads to intraoperative management of common bile duct with additional operating time. A systematic review assessed the difference between the different techniques for CBDS removal (i.e., preoperative ERCP with sphincterotomy, intraoperative ERCP with sphincterotomy, laparoscopic or open common bile duct exploration, or postoperative ERCP with sphincterotomy) and found no differences in terms of morbidity, mortality, and success comparing these methods [48]. For these reasons, CBDS could be removed preoperatively, intraoperatively, or postoperatively according to the local expertise and technique availability.

### 4.3.6 Alternative Treatments for High-Risk Patients

Cholecystectomy for ACC in the elderly and in high-risk patients has always been considered a high-risk procedure with a reported mortality up to 19% [49]. Gallbladder drainage, also known as percutaneous cholecystostomy (PC), is a potential alternative to cholecystectomy in high-risk patients, but its role is difficult to determine because different definitions are used to identify "high-risk" patients. PC decompresses the infected bile or pus in the gallbladder, removing the infected collection without removing the gallbladder. The removal of the infected material, in addition to antibiotic therapy, can result in reduced inflammation and improvement of the clinical condition. A recently published Dutch trial, the CHOCOLATE trial, compared the results of PC and laparoscopic cholecystectomy in high-risk patients with ACC [50]. The trial was concluded early after a planned interim analysis due to a significantly higher percentage (65% vs. 12%) of major complications in the percutaneous catheter drainage group compared to the laparoscopic cholecystectomy (RR 0.19, 95% CI 0.10-0.37, $p < 0.001$). In the drainage group, 66% of patients required a reintervention compared with 12% in the cholecystectomy group ($p < 0.001$). Recurrent biliary disease occurred more often in the percutaneous drainage group (53% v 5%, $p < 0.001$), and the median length of hospital stay was longer (9 days v 5 days, $p < 0.001$). These results are in favor of early laparoscopic cholecystectomy even for high-risk patients. However, it is important to note that the definition of high-risk patients in this trial included patients with APACHE II score between 7 and 15, while patients with an APACHE II score > 15 were excluded. Furthermore, other exclusion criteria were: symptoms that lasted longer than 7 days at time of first presentation, pregnancy, decompensated liver cirrhosis, admission to the intensive care unit at the time of cholecystitis diagnosis, and mental illness prohibiting informed consent. In this setting, the patients that could really have benefitted from percutaneous drainage are actually excluded from the trial, and the results of the study should be interpreted with the caveat of significant exclusion criteria. A previous Cochrane systematic review by Gurusamy et al. investigated the role of cholecystostomy. Authors included only two randomized trials, both at high risk of bias, concluding that "we are unable to determine the role of percutaneous cholecystostomy in the clinical management of high-risk surgical patients with acute cholecystitis" [51]. Furthermore, De Mestral et al. published a large retrospective epidemiological analysis in 2012 showing that only 40% of patient underwent delayed laparoscopic cholecystectomy after percutaneous drainage, and the 1 year readmission rate for patients who did not undergo delayed laparoscopic cholecystectomy was 49% with an in-hospital mortality of 1% [52]. In light of the above findings, a patient-tailored approach is the best choice, and percutaneous drainage can be considered as a possible alternative to surgery or after the failure of conservative treatment in a small subset of patients unfit for emergency surgery due to severe comorbidities. However, it is important to remember the complications associated with percutaneous drainage.

## 4.4 Conclusions

Based on the evidence included in these guidelines, it is clear that early laparoscopic cholecystectomy is the best therapeutic approach for ACC and that postoperative antibiotics are not necessary for uncomplicated cholecystitis. The most important takeaway of these guidelines is the superiority of early laparoscopic cholecystectomy for all patients among treatment options for ACC. According to several high-quality studies, subtotal cholecystectomy, along with a low threshold for conversion from complete cholecystectomy to partial or open approach, should be recommended when severe, acute inflammation of the gallbladder is encountered at time of operation. Although the threshold for conversion strongly depends on the experience and skills of the surgeon, we support the development of an intraoperative score to help the surgeon decide whether to complete the operation by partial cholecystectomy and/or by open approach when "the critical view of safety" cannot be reached without adding risk. The recommendations on the surgical treatment of ACC are limited to patients who are good candidates for urgent surgery. Gray areas still remain in cases of patients not fit for urgent surgery or for laparoscopic surgery secondary to general conditions. However, age alone is not a contraindication for surgery. These WSES guidelines define the patient condition in lieu of the cholecystitis severity score as underlined in the TG13. This approach could favor a therapy tailored to the patient's individual condition. Data on criteria for defining a patient as high-risk, besides septic shock, are scarce and of low quality. This is certainly an area for research to improve the management of patients with ACC. The role of cholecystostomy, as a bridging therapy until cholecystectomy or as a definitive treatment in elderly patients, is uncertain. The high incidence of major complications post-percutaneous drainage, as shown by the CHOCOLATE trial, is important to consider when evaluating this intervention as a possible alternative to surgery or after the failure of conservative treatment in the small subset of patients unfit for emergency surgery due to their severe comorbidities.

Moreover, studies providing a high level of evidence on the management of associated common bile duct stones (CBDS) have also been published. AUS is an accurate technique to visualize CBDS, and patients with a high likelihood of CBDS as seen on AUS should have a preoperative ERCP, while patients with a moderate risk should have a noninvasive preoperative investigation. Because the majority of RCTs exclude elderly patients, evidence has to be extrapolated from that in the younger population. This indirectness causes significant uncertainty in developing guidelines for management of acute cholecystitis in the elderly population. Future research on management of acute cholecystitis should include elderly patients whenever ethical and possible. In addition, researchers should present a subgroup analysis of the results in elderly patients, to resolve areas of uncertainty across age groups. The development and validation of a reliable prognostic score in assessing frailty would greatly help in guiding the management on acute calculous cholecystitis.

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# 5 Tokyo Guidelines and Their Limits

Kohei Mishima and Go Wakabayashi

## 5.1 Diagnostic Criteria and Severity Grading of Acute Cholecystitis

The diagnostic criteria and severity grading of acute cholecystitis (AC) were discussed among global experts at the Tokyo Consensus Meeting held in 2006, and the first version of Tokyo Guidelines (TG07) was published in 2007 [1]. TG07 diagnostic criteria was revised in 2013 as Tokyo Guidelines 2013 (TG13) [2] in response to a validation study [3] of TG07. According to a validation survey [4] of TG13, the TG13 diagnostic criteria for acute cholecystitis (Table 5.1) had higher sensitivity and specificity than those of TG07, and continuous use of TG13 criteria was recommended in the updated version of Tokyo Guidelines (TG18) [5]. Regarding the severity grading system, while TG07 defined Grade III (severe) AC as AC with indication for emergent surgery, the revised TG13 described Grade III AC as AC associated with organ system dysfunction, which in some circumstances may require treatment in an intensive care unit [2]. According to a case series study of over 5000 patients, the prognosis for Grade III patients was significantly worse than that for Grades I and II [4]. The TG 13 severity grading of acute cholecystitis (Table 5.2) was recommended for continuous use in the TG18 severity grading of acute cholecystitis as a useful indicator from the perspective of predicting prognosis [5].

**Table 5.1** TG18/TG13 diagnostic criteria for acute cholecystitis. From [5], with permission

| |
|---|
| A. Local signs of inflammation |
| (1) Murphy's sign, (2) RUQ mass/pain/tenderness |
| B. Systemic signs of inflammation |
| (1) Fever, (2) elevated CRP, (3) elevated WBC count |
| C. Imaging findings characteristic of acute cholecystitis |
| Suspected diagnosis: one item in A + one item in B |
| Definite diagnosis: one item in A + one item in B + C |

## 5.2 Flowcharts for the Management of Acute Cholecystitis

### 5.2.1 Revisions of Flowcharts for the Management

Flowcharts for the management of acute cholecystitis (AC) were presented in TG07 [6] and revised in TG13 [7]. These flowcharts were useful to show recommended treatments according to the severity of AC. However, TG07 and TG13 did not cover issues like physical status, comorbidities, or other risk factors when choosing a treatment pathway according to severity. In

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addition, Grade III AC was considered not suitable for straightforward laparoscopic cholecystectomy (LC). In the TG18 guidelines [8], modified flowcharts (Figs. 5.1, 5.2, and 5.3) were proposed based on recent recommendations in the clinical setting and evidence reported after the publication of TG13 [9, 10]. The revision of flowcharts was aimed at improving the percentage of lives saved by allowing clinicians to determine how they can safely treat AC through the use of decision-making criteria even for severe cases.

**Table 5.2** TG18/TG13 severity grading for acute cholecystitis. From [5], with permission

| |
|---|
| Grade III (severe) acute cholecystitis is associated with dysfunction of any one of the following organs/systems: |
| 1. Cardiovascular dysfunction: hypotension requiring treatment with dopamine ≥5 μg/kg per min, or any dose of norepinephrine |
| 2. Neurological dysfunction: decreased level of consciousness |
| 3. Respiratory dysfunction: PaO2/FiO2 ratio < 300 |
| 4. Renal dysfunction: oliguria, creatinine >2.0 mg/dl |
| 5. Hepatic dysfunction: PT-INR >1.5 |
| 6. Hematological dysfunction: platelet count <100,000/$mm^3$ |
| Grade II (moderate) acute cholecystitis is associated with any one of the following conditions: |
| 1. Elevated WBC count (>18,000/$mm^3$) |
| 2. Palpable tender mass in the right upper abdominal quadrant |
| 3. Duration of complaints >72 ha |
| 4. Marked local inflammation (gangrenous cholecystitis, pericholecystic abscess, hepatic abscess, biliary peritonitis, emphysematous cholecystitis) |
| Grade I (mild) acute cholecystitis does not meet the criteria of Grade III or Grade II acute cholecystitis |

### 5.2.2 The Updated Version of Tokyo Guidelines (TG18)

The selection of treatment strategy for patients at each severity grade was based on risk factors [8]. The risk factors adopted in TG18 were: Charlson comorbidity index (CCI) score [9] and the American Society of Anesthesiologists physical status classification (ASA-PS) score [10]. Early LC to treat AC of moderate and severe grades (Grade II and III) should be performed only at advanced centers where experienced surgeons practice. An advanced center should have both appropriate personnel and facilities to manage the level of patients being managed. Surgeons should have experience in advanced laparoscopic techniques, and intensive care unit should be available. LC can be performed to treat AC if the conditions described above for each Grade are satisfied.

### 5.2.3 Definition of Early Cholecystectomy

TG07 recommended that surgery for AC be performed soon after hospital admission, whereas TG13 recommended that surgery be performed soon after admission and within 72 h after onset. When managing AC, it is difficult to determine precisely how many hours have passed since disease onset. The meta-analysis of the case study reports [11] found that compared with delayed cholecystectomy, early cholecystectomy for cases within 72 h of patient presentation or symptom onset was associated with lower mortality rates, complication rates, incidence of bile duct injury, and switching to open surgery.

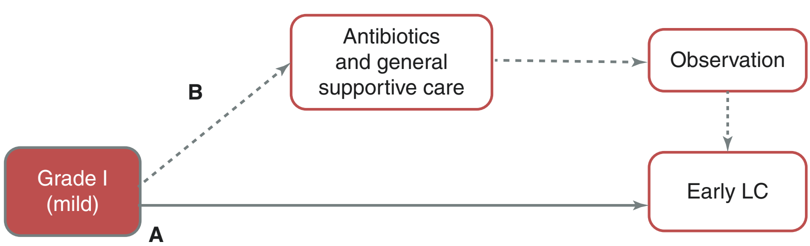


**Fig. 5.1** TG18 flowchart for the management of Grade I AC [8]. A, CCI 5 or less and/or ASA class II or less (low risk); B, CCI 6 or greater and/or ASA class III or greater (not low risk)

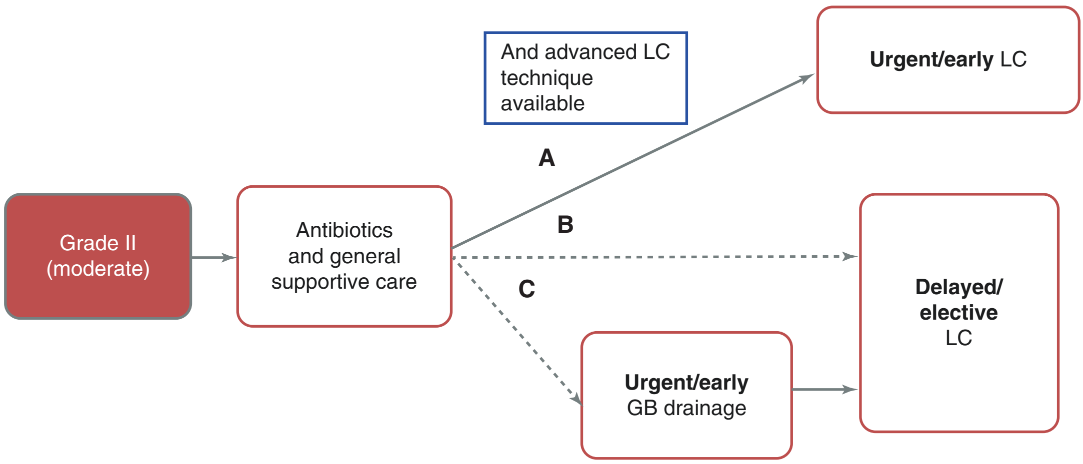


**Fig. 5.2** TG18 flowchart for the management of Grade II AC [8]. A, CCI 5 or less and/or ASA-PS class II or less (low risk); B, CCI 6 or greater and/or ASA-PS class III or greater (not low risk); C, antibiotics and general supportive care fail to control inflammation

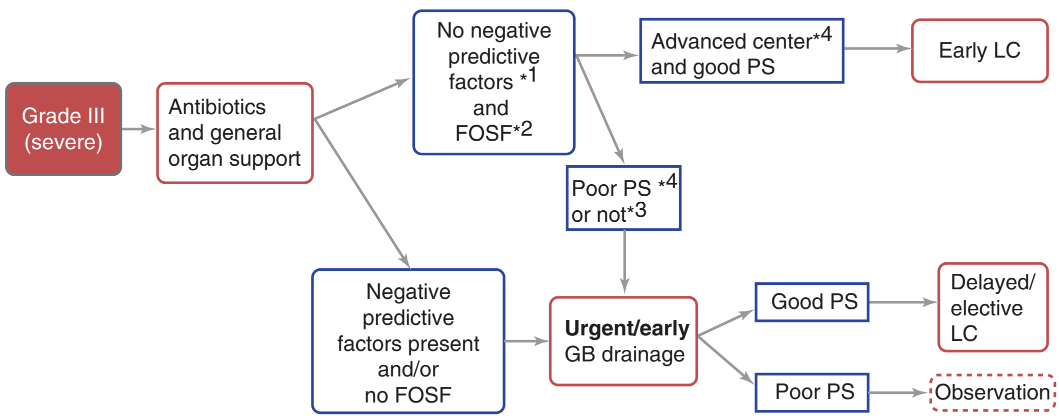


**Fig. 5.3** TG18 flowchart for the management of Grade III AC [8]. *1, negative predictive factors = jaundice (TBil ≥2), neurological dysfunction, respiratory dysfunction; *2, FOSF: favorable organ system failure = cardiovascular or renal organ system failure which is rapidly reversible after admission and before early LC in AC; *3, advanced center = intensive care and advanced laparoscopic techniques are available; *4, poor PS = CCI (Charlson comorbidity index) 4 or greater, ASA-PS 3 or greater

Similar results were also obtained with early cholecystectomy for cases with time from onset 72 h to 1 week [12, 13]. Therefore, TG 18 recommended early surgery regardless of exactly how much time has passed since onset, if a patient is deemed capable of withstanding surgery for AC.

## 5.3 Surgical Management of Acute Cholecystitis

Compared to TG13, TG18 recommended that clinicians should consider early LC even for moderate or severe AC [8]. The backbone of this change was the improvement of the operative skill for early

LC and perioperative care. Regarding the improvement in operative skills, standardized procedures of safe LC were proposed [14]. The critical view of safety (CVS) is the most important concept in the safe LC [15]. Several landmarks are helpful for surgeons to safely proceed surgical procedures during the process for the establishment CVS. The baseline of the segment 4 of the liver and the Rouviere's sulcus are good landmarks for the start line of dissecting the serosa of gallbladder for avoiding the bile duct injury of the anterior and posterior branch of Glissonian pedicles [14]. A bailout procedure should be chosen when a CVS cannot be achieved because of the presence of severe fibrosis.

## 5.4 Management Strategies for Gallbladder Drainage

A standard drainage method for surgically high-risk patients with AC and the latest developed endoscopic gallbladder drainage techniques were described in the updated Tokyo Guidelines 2018 (TG18) [16]. Percutaneous transhepatic gallbladder drainage (PTGBD) should be considered the first alternative to surgical intervention in surgically high-risk patients with AC. Also, endoscopic transpapillary gallbladder drainage or endoscopic ultrasound-guided gallbladder drainage can be considered in high-volume institutes by skilled endoscopists.

## 5.5 The Limits of TG18

### 5.5.1 Introduction

Tokyo Guidelines flowcharts allow clinicians to understand treatment flow at a glance and have proven useful standardization of the management of AC [8]. There have been significant changes in clinical management, including advances in surgical techniques [14] and equipment and progress in multidisciplinary treatment [16]. However, there are still issues warranting resolution.

### 5.5.2 Is Early LC Feasible for Patients with Grade III AC?

The severity grading of TG18/13 [5] is regarded as a useful classification system to predict the mortality rate of AC [4]. TG18 flowcharts [8] recommended that early LC or GB drainage following initial systemic treatment be performed for patients with Grade III AC. However, it is difficult for clinicians to choose early LC for Grade III AC according to TG18 flowchart, since the flowchart did not include elements of surgical difficulty and accompanying cholangitis. Although bailout procedures can be performed in difficult cases [14], conversion from LC to open surgery and postoperative complications are significantly more likely for patients at higher severity grades [17, 18]. A set of severity grading criteria including surgical difficulty is needed to be produced in the future.

### 5.5.3 How to Manage Elderly Patients with AC?

The management of elderly patients with AC is still a complex challenge due to the balance of benefits from LC versus the increased risk of perioperative morbidity and mortality [13]. In TG18 flowcharts [8], ASA-PS and age-adjusted CCI were adopted to evaluate physical status of patients, and age-adjusted CCI $\geq 6$ and ASA-PS $\geq 3$ were proposed as surgical risk factors based on the result of a cohort study [9]. Most elderly patients are classified into high-risk patients in this criteria. On the other hand, one study reported no deaths after cholecystectomy for patients with ASA-PS $\geq 3$ at advanced centers [19]. In the era of aging society, AC in elderly patients is becoming an increasingly frequent problem. More case series data is needed to be gathered for future analysis to compare the clinical outcomes of early LC in high-risk elderly patients and those of conservative therapy with or without PTGBD.

### 5.5.4 What Determines the Advanced LC Technique?

In the 1990s, AC is regarded as contraindicated for LC according to SAGES guidelines [20]. But as times have changed, advances in optical and surgical devices and improvements in surgical techniques have led to the expansion of indications for LC [14]. As LC for AC has been more widely performed, vasculo-biliary injury is known to occur in a certain population of cases [21]. Therefore, TG18 flowcharts [8] recommended that early LC for AC be performed by surgeons with advanced techniques at advanced centers. In addition, the chapter of surgical management of AC was added to describe safe steps in LC for AC [14]. However, clinical evidence is scarce on advanced techniques of LC at the moment and warrants further investigation.

### 5.5.5 Summary

Based on studies that have found the lifespan of guidelines to be around 5 years [22], the Tokyo Guidelines Revision Committee revised the guidelines in 2013 and 2018. TG18 should be validated from abovementioned viewpoints during the next several years and be revised according to newly published clinical evidence.

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# 6 Preoperative Evaluation and Management of Acute Cholecystitis: Optimal Timing and Surgical Approach

Wesley Wendell B. Cruz and Ho-Seong Han

## 6.1 Introduction

Acute cholecystitis is defined as inflammation of the gallbladder, mainly due to bile obstruction with or without bacterial proliferation. Over 90% of cases are caused by an obstructing stone at the level of the cystic duct [1, 2]. Other causes include helminthic infections such as ascariasis, enlarged cystic node, or tumors [3]. Persistence of the inflammation and distention often leads to severe complications including hydrops, empyema, gangrene, and perforation, which if left untreated may lead to increased mortality and morbidity [4]. Ultrasound is the initial imaging of choice for patients with suspected acute cholecystitis. In equivocal cases, HIDA scan is preferred over MRI or CT scan due to its higher sensitivity and specificity. Guidelines have been established and validated in the diagnosis, treatment, and management of acute cholecystitis [5–7].

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## 6.2 Etiology and Pathogenesis

Gallstone formation has dated back as early as 3500 BC, as recorded from Egyptian and Chinese autopsies [8]. Bile, which is synthesized by the liver, is secreted and subsequently stored in the gallbladder. During storage, the gallbladder concentrates the bile, absorbing most of its water content. The bile is then secreted from the gallbladder, aiding in digestion. Alterations in absorption, such as oversaturation and concentration of bile, may precipitate its solid contents, thus forming biliary stones [9].

The most common cause of acute cholecystitis is an impacted stone at the level of the cystic duct or infundibulum. In developing countries in Asia, southern Africa and Latin America, helminthic infections (ascariasis) may also be commonly encountered [3]. Uncommon causes of cholecystitis may include strictures, kinking of the cystic duct, intussusception of a polyp, torsion of the gallbladder, or external compression from an overlying lymph node on the cystic duct [4].

In adults, approximately 10–20% will develop gallstones during their lifetime. Risk factors which may contribute to stone formation include family history, genetics, female sex, ethnicity, age, obesity, use of certain drugs, rapid weight loss and presence of other underlying diseases such as liver cirrhosis and Crohn's disease [8, 9].

Majority of cases are usually asymptomatic, with only ~20% presenting with symptoms such as abdominal pain, fever, nausea and/or vomiting.


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Abdominal pain may be characterized as persistent, localized in the right upper quadrant or epigastric area, with radiation to the right shoulder and back. Pain in cholecystitis is believed to be caused by increase in intraluminal pressure within the gallbladder due to an obstructing stone, leading to gallbladder distention. As a result of this distention, blood vessels within the gallbladder wall may be compressed, leading to ischemia and gangrene, with the most common site being the gallbladder fundus [10]. If left untreated, this may lead to gallbladder perforation and subsequent abscess formation or peritonitis, with complication rates as high as 22% and 16–25%, respectively [11].

Fever and leukocytosis (WBC >10,000/μL) are also usually seen in acute cholecystitis. Aside from causing obstruction, the gallstones itself may contribute to the inflammatory response by stimulating prostaglandins $I_2$ and $E_2$. Bacterial proliferation, found in 20% of cases of acute cholecystitis, is usually caused by Gram negative bacteria of gastrointestinal origin, such as *Klebsiella spp*. and Escherichia coli.

## 6.3 Imaging

Transabdominal ultrasound is the preferred initial imaging test for patients suspected to have acute cholecystitis, since it is readily available, inexpensive, and noninvasive [10, 11]. A diagnosis of acute cholecystitis may be reached based on ultrasonographic findings of: (1) impacted gallstones at the infundibulum or cystic duct; (2) gallbladder wall diameter of >4 mm; (3) fluid collection around the gallbladder; and (4) gallbladder diameter of >8 cm (long axis) × >4 cm (short axis) [12]. Sensitivity of ultrasound in the detection of acute cholecystitis is relatively high at 84%, with a positive sonographic Murphy's sign increasing the sensitivity to as much as 92%. Specificity is also high at 99% (97–100%) [9, 11, 12]. Aside from diagnosing cholecystitis, ultrasound also has high sensitivity in detecting gallbladder stones (92%) [13, 14].

Cholescintigraphy or hepatic 2,6-dimethyliminodiacetic acid (HIDA) scan (Fig. 6.1) is considered to be the "gold standard" in diagnosing acute cholecystitis. In HIDA scan, a radioactive tracer is injected intravenously, subsequently taken up by the liver and excreted into the bile ducts. The tracer is stored in the gallbladder for approximately 30 min after administration. A normal scan would demonstrate the liver, bile ducts, gallbladder, and duodenum after 1 h of administration; thus, non-visualization of the gallbladder and the cystic duct may indicate an impacted stone or obstruction at the cystic duct (Fig. 6.2). The sensitivity and specificity of HIDA scan in diagnosing acute cholecystitis is higher compared to ultrasound (97% vs 96% and 98% vs 90%, respectively) [15–18]. However, the main disadvantage of this imaging modality is the exposure to ionizing radiation, as well as its cost and availability.

A study conducted by Cho et al. last 2011 demonstrated HIDA scan as a predictive tool for assessing the severity of acute cholecystitis. In the study, acute cholecystitis was diagnosed when two or more clinical and operative findings were present. Clinical findings included: temperature >37.5 °C, leukocytosis >10,000/μL, right upper quadrant pain and tenderness, and symptom duration >48 h; whereas operative findings included: gallbladder wall >4 mm, presence of severe adhesions, distorted biliary anatomy, and gross inflammation of the gallbladder fossa. Results showed that non-visualization of the gallbladder during HIDA scan was seen in 86.4% of the patients diagnosed as acute cholecystitis. In cases of complicated acute cholecystitis (such as hydrops, empyema, pericholecystic abscess, and gangrenous gallbladder), the diagnostic accuracy of HIDA scan was higher at 92.7%, compared to 75.3% of uncomplicated acute cholecystitis. Gallbladder ejection fraction (GBEF) (Fig. 6.1d) was also included and shown to have a predictive value of 82.9%. A GBEF of <30% was significantly associated with increased difficulty during laparoscopic cholecystectomy, with associated increase in operative time, blood loss, and postoperative complication rates compared to those with GBEF 30% or higher (6.3% vs 2.6%; $p = 0.006$) [19].

In comparison, MRI with MRCP with or without contrast has been shown to have higher sensi-

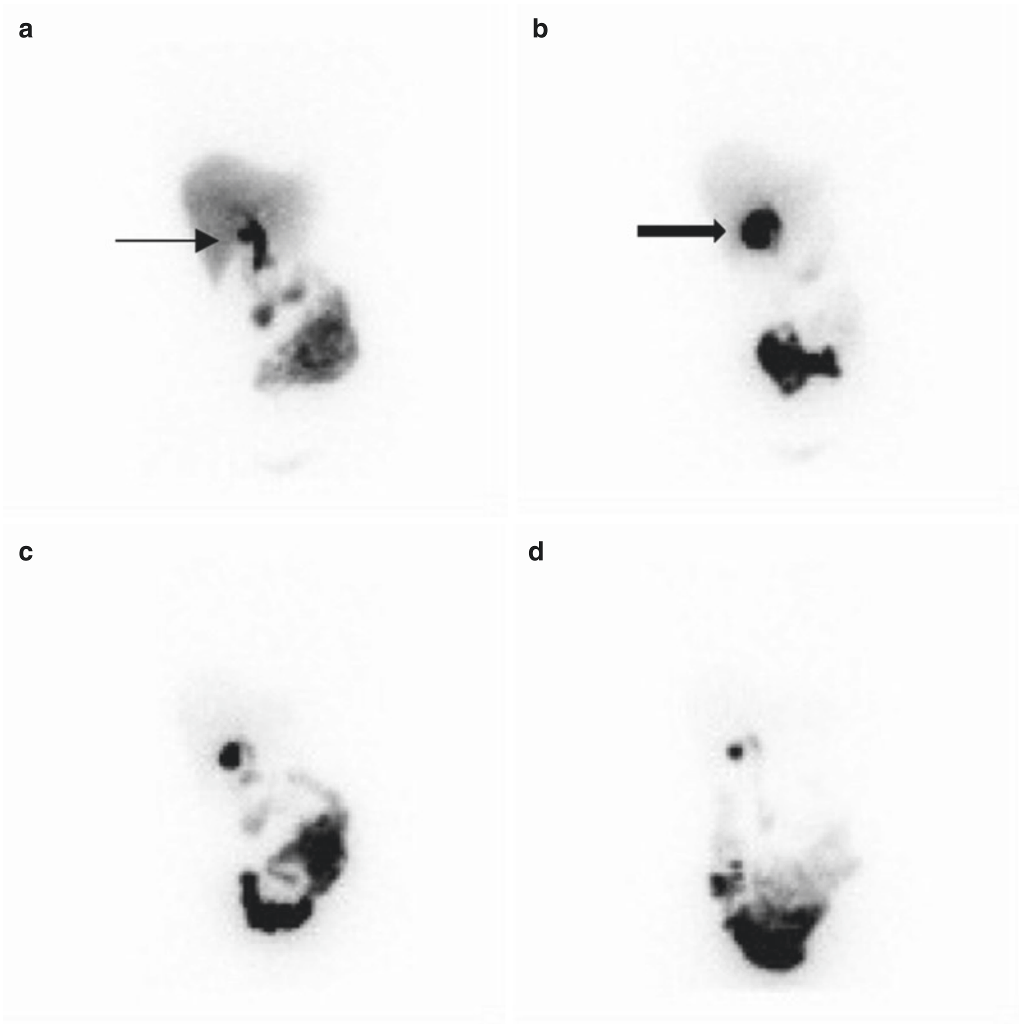


**Fig. 6.1** HIDA scan of a 46-year-old female, (**a**) patent cystic duct at 30 min with normal liver uptake (narrow arrow), (**b**) visualized gallbladder at 60 min (thick arrow), (**c**) tracers are seen in the small bowel at 90 min, (**d**) retention of tracer in the gallbladder and common bile duct with ejection fraction (GBEF) of 73.25%

tivity than ultrasound at 85% but lower than that of HIDA scan [20]. MRI is able to detect inflammation, fluid retention, and fatty tissues around the gallbladder, while MRCP is able to provide images of the biliary tree even without contrast. Thus, MRI has been recommended as the diagnostic imaging of choice when ultrasound results are equivocal.

Use of CT scan in the diagnosis of acute cholecystitis is limited, since ultrasound and HIDA scan both have higher sensitivities in diagnosing suspected acute cholecystitis. As demonstrated in a study conducted by Fagenholz et al. (2015), ultrasound had a higher sensitivity in detecting gallbladder stones compared to CT scan (87% vs 60%, $p < 0.01$) [13, 21]. However, CT scan is still useful in diagnosing gangrenous cholecystitis, with relatively high diagnostic accuracy at 87.6%. It also has high specificity in the detection of presence of gas in the lumen or wall (100%), irregular or absent walls (97.6%), and abscess formation (96.6%) [22, 23].

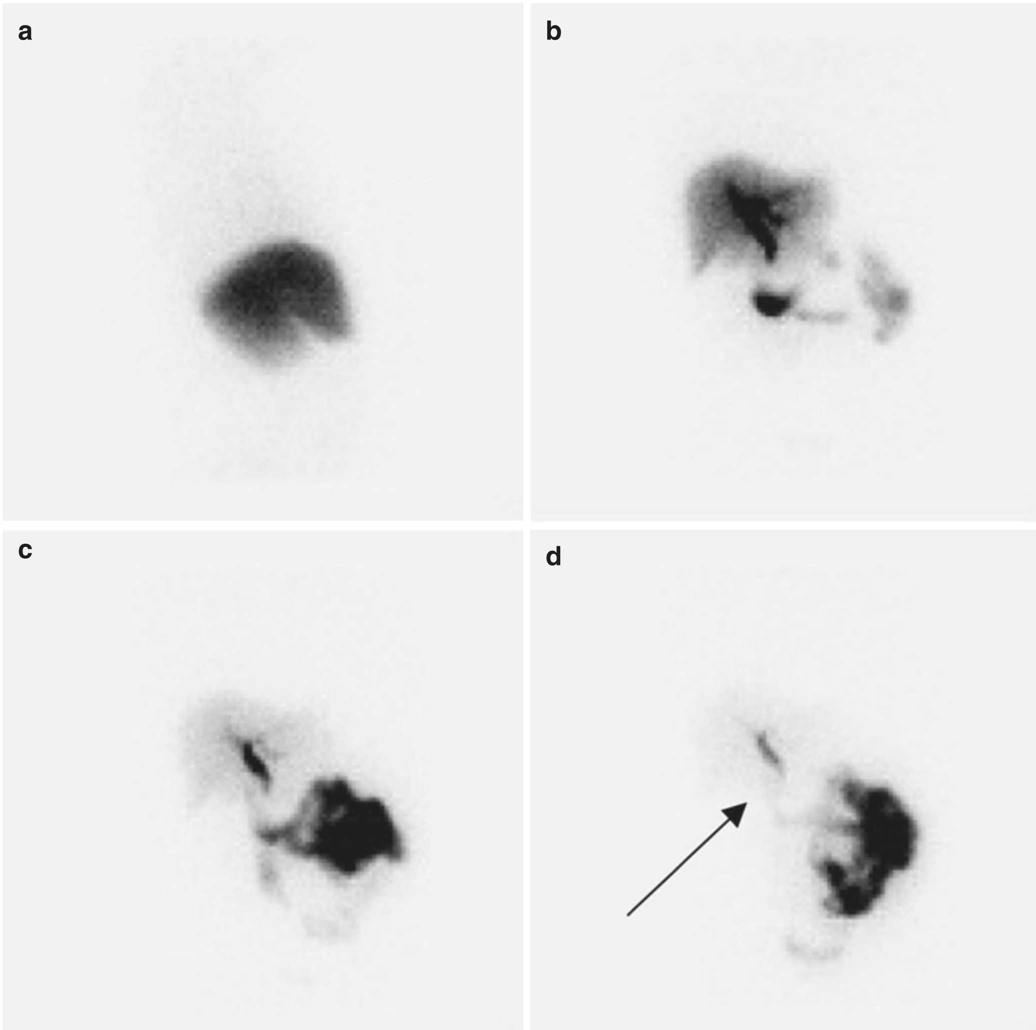


**Fig. 6.2** HIDA scan of a 58-year-old male, (**a**) tracers with normal liver uptake, (**b**) tracers shown highlighting the main intrahepatic ducts and common bile duct at 30 min, (**c**) tracers are seen in the small bowel with some retention in the common bile duct, (**d**) most tracers are seen in the small bowel with decrease amount in the common bile duct. Non-visualization of the gallbladder and cystic duct up to 3 h (narrow arrow)

## 6.4 Diagnosis and Severity Grading

Prior to 2007, standard diagnostic criteria for acute cholecystitis were not available. Clinical history, physical examination, and routine laboratory tests were primarily used, resulting in a number of unnecessary cholecystectomies or missed diagnoses [10].

### 6.4.1 Diagnosis

In 2007, global experts at the Tokyo Consensus Meeting met and established the first version of the Tokyo Guidelines for the diagnosis, severity grading, and management of acute cholecystitis (TG7); in 2013, these guidelines were revisited and revised according to current literature and validity studies, and TG13 guidelines were

**Table 6.1** TG18/13 Diagnostic Criteria for Acute Cholecystitis. From [5], with permission

| |
|---|
| A. Local signs of inflammation |
| (1) Murphy's sign |
| (2) Right upper quadrant mass/pain/tenderness |
| B. Systemic signs of inflammation |
| (3) Fever |
| (4) Elevated CRP |
| (5) Elevated WBC count |
| C. Imaging findings |
| (6) Imaging findings characteristic of acute cholecystitis |
| *Definitive diagnosis*: one item in A + one item in B + C |
| *Suspected diagnosis*: one item in A + one item in B |

Acute hepatitis, other acute abdominal diseases, and chronic cholecystitis should be excluded
*WBC* white blood count, *CRP* C-reactive protein

released. In 2017, Yokoe and Takada conducted a validation study on TG13 and demonstrated that the TG13 guidelines were useful in definitively diagnosing acute cholecystitis, with a sensitivity of 84.9%, but low specificity at 50.0%. These issues were then addressed in the revision of TG13, and subsequent numerous validation studies of TG13 in clinical practice have yielded higher sensitivity and specificity rates of 91.2% and 96.9%, respectively, with concomitant increase in accuracy rate from 92.7% to 94.0%; thus, these recommendations were adopted into the latest Tokyo Guidelines for 2018 (TG18) without any modification [5].

According to TG18, a definitive diagnosis of acute cholecystitis is made if all of the following criterion are met: Presence of local signs of gallbladder inflammation (A), presence of systemic signs of inflammation (B), and imaging findings characteristic of acute cholecystitis (C) (Table 6.1). Acute cholecystitis is suspected if local (A) and systemic (B) signs of inflammation are present but is not supported by any of the imaging modalities done (ultrasound, CT scan, or MRI).

### 6.4.2 Severity Assessment

Once the diagnosis of acute cholecystitis is made, the patients should then be categorized according to the severity of the disease (Table 6.2). Severe cholecystitis (Grade III) is defined as acute cholecystitis accompanied with end organ failure (cardiac, neurologic, pulmonary, renal, hepatic, or hematologic failure). Moderate cholecystitis (Grade II) should include any of the following conditions: signs of local inflammation, duration of signs and symptoms >72 h, a palpable tender mass at the right upper quadrant during physical examination, or leukocytosis of 18,000/mm$^3$. If the criterion for severe or moderate cholecystitis is not met, then the patient is categorized as mild cholecystitis [5].

**Table 6.2** TG18/TG13 Severity Grading for Acute Cholecystitis. From [5], with permission

| Grade III (severe) acute cholecystitis |
|---|
| "Grade III" acute cholecystitis is associated with dysfunction of any one of the following organs/systems:<br>1. Cardiovascular dysfunction: hypotension requiring treatment with dopamine ≥5 lg/kg per min, or any dose of norepinephrine<br>2. Neurological dysfunction: decreased level of consciousness<br>3. Respiratory dysfunction: $PaO_2/FiO_2$ ratio < 300<br>4. Renal dysfunction: oliguria, creatinine >2.0 mg/dl<br>5. Hepatic dysfunction: PT-INR >1.5<br>6. Hematological dysfunction: platelet count <100,000/mm$^3$ |
| **Grade II (moderate) acute cholecystitis** |
| "Grade II" acute cholecystitis is associated with any one of the following conditions:<br>1. Elevated WBC count (>18,000/mm$^3$)<br>2. Palpable tender mass in the right upper abdominal quadrant<br>3. Duration of complaints >72 h<br>4. Marked local inflammation (gangrenous cholecystitis, pericholecystic abscess, hepatic abscess, biliary peritonitis, emphysematous cholecystitis) |
| **Grade I (mild) acute cholecystitis** |
| "Grade I" acute cholecystitis does not meet the criteria of "Grade III" or "Grade II" acute cholecystitis. It can also be defined as acute cholecystitis in a healthy patient with no organ dysfunction and mild inflammatory changes in the gallbladder, making cholecystectomy a safe and low-risk operative procedure |

*$PaO_2$* partial pressure of oxygen, *$FiO_2$* fraction of inspired oxygen, *PT-INR* prothrombin time-international normalized ratio, *WBC* white blood count

#### 6.4.2.1 Other Possible Factors to Be Considered in the Diagnosis and Severity Grading of Patients with Acute Cholecystitis

Preoperative assessment is a vital step in the approach of a patient with suspected acute cholecystitis, since several factors may contribute to increased risk and predisposition for acute cholecystitis. Cho et al. in 2010 identified risk factors which increased the risk for development of acute cholecystitis in patients with gallbladder stones ($p < 0.0001$) [24]. These factors included: (1) presence of comorbidities (cardiovascular disease, diabetes, and cerebrovascular accident (CVA); (2) age >60 years old; and (3) male gender [24, 25]. The study concluded that presence of these factors may be associated with early development of complications of acute cholecystitis.

Onoe et al. in a review of acute cholecystitis cases diagnosed according to TG18/TG13 proposed a predictive scoring system that would determine ease of achieving the critical view of safety based on preoperative factors. The following three factors were considered: (1) C-reactive protein >5.5 mg/dl (3 points); (2) symptom duration >72 h (2 points); and (3) impacted gallstones (1 point) on imaging. The higher the points, the less likely the critical view of safety (CVS) was identified during laparoscopic cholecystectomy ($p < 0.001$) [26]. Other risk factors proposed to be predictive of difficulties during cholecystectomy were ASA score > III ($p < 0.001$) and those with concomitant common bile duct (CBD) stones ($p < 0.001$) [27].

## 6.5 Treatment

The aim of treatment in patients diagnosed with acute cholecystitis is stabilization and optimization prior to definitive intervention. Resuscitation with intravenous fluids and correction of electrolytes is the initial step. The patient is placed on NPO (nothing-per-orem) as oral intake may aggravate contraction of the gallbladder, producing more pain. H2-blockers or Proton-pump inhibitors are started. Analgesics should be initiated, preferably nonsteroidal anti-inflammatory drugs (NSAIDS) to inhibit the cyclooxygenase pathway (Cox-1 and Cox-2) and decrease the mucous production in the gallbladder [7].

Initiation of anti-microbial empiric therapy for acute cholecystitis is dependent on severity grading. In mild (Grade I) acute cholecystitis, antibiotic therapy is recommended prior to surgery. In moderate (Grade II) and severe (Grade III) acute cholecystitis, antibiotics should be given once the diagnosis is made. In TG18/13, it is recommended that antibiotics be started immediately (within 1 h) for severe cases and urgently (within 6 h) for moderate cases [7]. Antibiotic treatment should be directed to the microorganisms of the gut, most commonly *Escherichia coli*, *Klebsiella spp*, *Enterococcus spp*., and the anaerobic organisms [28–32]. Bile samples should be taken for microbial culture and antibiotic sensitivity testing, and antibiotics promptly shifted once bile culture results become available [29]. Blood culture is not necessary unless warranted [28].

For mild and moderate cases, antibiotics should be stopped once source control (cholecystectomy) has been achieved. Several randomized control trial studies regarding continuation of antibiotics postoperatively showed no benefit in extending antibiotics in terms of decrease in postoperative infections [33, 34], and this has been supported by meta-analyses [35, 36]. It was also demonstrated from these meta-analyses that prolonged administration of antibiotics in fact lengthened hospital stay, increased overall costs, and increased microbial resistance [35, 36]. For severe cholecystitis cases, antibiotics are recommended to be continued for a duration of 4–7 days after cholecystectomy [7, 28].

### 6.5.1 Timing: Early vs Delayed Cholecystectomy

It has been a long-standing debate on whether surgery for acute cholecystitis be done during the same admission or after a prolonged interval, and up to the present time there is still some controversy in deciding between early and delayed cholecystectomy [37]. By definition, early cholecystectomy may range from time of admission up to 10 days from onset of the symptoms [38–40], while delayed cholecystectomy is defined as surgery scheduled 6–8 weeks after the initial symptoms with administration of antibiotics, with the rationale that at this time most of the inflammatory process has subsided.

In Tokyo Guidelines 2018/2013, early laparoscopic cholecystectomy (defined as 72 h to 1 week after onset of symptoms) was compared to delayed cholecystectomy in terms of operative time, bile duct injuries, length of hospital stay, and overall cost of treatment. It was determined that there was no statistical difference in outcomes between the early and delayed groups [7].

A meta-analysis done by Lyu et al., composed of 15 randomized trials with 1669 patients, compared early laparoscopic cholecystectomy and delayed laparoscopic cholecystectomy [39]. The primary outcomes considered were risk for bile duct injury and bile leak, and secondary outcomes included wound infection, complications, conversion to open cholecystectomy, and operative time. It was determined that there was no significant difference between the two treatment groups in terms of increased risk for bile leak and bile duct injuries, as well as the included secondary outcomes (wound infection, complications, and operative time). Postoperative length of stay also showed no difference between the two groups. A subgroup analysis was also performed, wherein early laparoscopic cholecystectomy was divided into three groups (3 days, 4 days, and 7 days from onset of symptoms) and then compared to delayed cholecystectomy. Even in subgroup analysis, the 3-day and 4-day groups showed no difference in terms of operative time; however, the 7-day group showed a longer operative time compared to the delayed group [39].

Early cholecystectomy for acute cholecystitis is therefore a safe and feasible option, regardless of severity grading, and this has been consistently supported by various trials and meta-analyses [37, 38, 40–46]. Aside from comparable outcomes between early and delayed intervention, early cholecystectomy also decreases the risk for recurrence of symptoms, total hospital cost, and total hospital stay.

#### 6.5.1.1 Timing of Early Cholecystectomy: What Is "Early?"

As was previously stated, early surgery has been defined to range from the day of admission (onset of symptoms) to as long as the tenth hospital day. Blohm et al. (2017) analyzed data from 15,760 cholecystectomies performed for acute cholecystitis within an 8-year period. It was noted that adverse events increased as surgery was delayed, with complications the least in cholecystectomies done within 2–3 days from admission [47]. A 30-day and 90-day mortality risk was noted to be reduced for patients who were operated on within three days of admission. A similar study done by Polo et al. in 2015 assessed the optimal timing of early cholecystectomy for acute cholecystitis. It was discovered that on patients where cholecystectomy was performed on the day of admission and 3 days after admission, mortality and morbidity (postoperative sepsis, ICU admission, and reoperation) increased significantly. It was suggested that in the first 24 h of admission, patients often present with unstable hemodynamics, and therefore require initial resuscitation and stabilization prior to any surgical intervention [47, 48]. It has thus been recommended that early cholecystectomy be done within the first three days, after initial resuscitative measures have been instituted [47–49].

### 6.5.2 Laparoscopic Cholecystectomy for Acute Cholecystitis

Surgical removal of the gallbladder, or cholecystectomy, is the definitive treatment for acute cholecystitis. From the first recorded open cholecystectomy performed in July 1882 by Dr. Carl Langenbuch in Lazarus Hospital, Berlin, it has since become the gold standard treatment for benign gallbladder diseases [50, 51]. In September 12, 1985, Prof Dr. Med Erich Mühe of Böblingen, Germany, performed the first laparoscopic cholecystectomy [52]. With this novel approach, open cholecystectomy has then slowly shifted to laparoscopic cholecystectomy over the past decades, emerging as the current gold standard in the treatment of benign gallbladder diseases [53].

As stated in TG18/13, laparoscopic cholecystectomy is a safe approach for the treatment of mild (Grade 1) and moderate (Grade 2) acute cholecystitis. In a study conducted by Keus et al. which included 38 randomized control trials (2338 patients), there was no significant difference between open cholecystectomy and laparoscopic cholecystectomy in terms of complications and mortality [54]. The advantages of the laparoscopic group seen in the study were shorter operative time, shorter hospital stay, decreased requirement for postoperative analgesics, and decreased morbidity [55].

Safety within the confines of the operating room theater, of both the patient and the surgeon, has always been the primary concern and priority in any field of surgery [56, 57]. Strasberg's analysis and review was the first to describe the critical view of safety (CVS) as an intraoperative tool during laparoscopic cholecystectomy to decrease bile duct and vascular injury [58–61]. As was stated by Strasberg, the CVS is achieved by opening up the triangle of Calot (clearance of fibrous and fatty tissues and separation of the lower third of the gallbladder from the liver to expose the liver surface, with no structures being ligated or divided), until only two structures are seen going to the gallbladder, the cystic duct, and the cystic artery [58].

However, in cases of acute cholecystitis with concomitant intense inflammation around the gallbladder and hepatoduodenal ligament surrounding the biliary tree, difficult cholecystectomy during laparoscopy may be an unavoidable encounter, whether timing of surgery be early or delayed. Identification of the critical view of safety may therefore be quite a challenge in the face of an ongoing inflammatory process, wherein the distorted anatomy poses a significant risk for vasculo-biliary injuries (VBI) [58].

Several intraoperative imaging strategies are available which may be utilized in the identification of the vital structures and CVS. Intraoperative cholangiography (IOC) may be used to identify the cystic duct and its junction with the common bile duct. In cases where biliary injury may have already occurred, IOC may also help in identifying early injuries. Intraoperative indocyanine green (ICG) may also be used to identify the biliary anatomy. However, the main limitation of ICG is the presence of severe inflammation, which may preclude clear visualization of the ducts [62]. Intraoperative ultrasound may also be used for intraoperative assessment of the vascular and biliary anatomy [56].

In instances where a difficult laparoscopic cholecystectomy is encountered (and absence of available intraoperative imaging modalities or lack of expertise) and a critical view of safety cannot be achieved, bailout techniques were developed. Partial or subtotal cholecystectomy may be performed, wherein partial removal of the gallbladder fundus and body may be carried out, with closure of the gallbladder remnant done using a reconstituting (complete closure of the gallbladder remnant) or fenestrated (open gallbladder with closure of cystic duct) technique. Fundus first (dome-down) technique is also another option for the difficult gallbladder. If the extrahepatic biliary anatomy cannot be identified, the surgeon may proceed to partial or subtotal cholecystectomy after a fundus first approach. In terms of a difficult laparoscopic surgery, conversion to open is another bailout approach; however, studies demonstrate that conversion does not lower the risk of VBI but increases it by a hundredfold [63].

In cases of Grade II and Grade III acute cholecystitis, TG18/13 recommends that open cholecystectomy be the preferred approach, especially for the less experienced surgeons [7]. This approach is also reserved for patients who cannot tolerate laparoscopic surgeries.

In conclusion, it is still the prerogative of the attending surgeon to perform whatever approach, technique, or combinations of techniques applicable in the current situation, as long as patient safety is paramount [56, 57].

#### 6.5.2.1 Other Treatment Alternatives Besides Cholecystectomy

Cholecystectomy may not always be an ideal option for a select group of patients. In patients with severe acute cholecystitis necessitating prolonged resuscitation with fluids and antibiotics, in patients with underlying medical conditions wherein general anesthesia is contraindicated, and in high-risk surgical patients, other techniques are recommended prior to definitive treatment [7]. Percutaneous biliary aspiration, with or without tube placement, to drain the infected bile contents can be done under local anesthesia either with or without sedation. Preferably, image-guided transhepatic gallbladder drainage is recommended due to less complications compared to percutaneous tube cholecystostomy. Another suggested method may be endoscopic transpapillary gallbladder drainage, but these are reserved for centers with an experienced endoscopist. Another safe and feasible approach is endoscopic ultrasound-guided gallbladder drainage through the antrum or bulb of the duodenum. A plastic stent or self-expanding metallic stent is then placed for internal drainage [64]. Once the patient recovers, elective cholecystectomy is then scheduled, either in the same admission or delayed setting (6–8 weeks).

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# 7 Perioperative Evaluation and Decision-Making, When to Operate and by Which Approach: Tube Cholecystostomy

Anthony Bacon, Travis Corgan, Tyler Pender, and Alexander Colonna

## 7.1 Introduction

Percutaneous cholecystostomy tubes (PCTs) have emerged as a safe and accepted therapeutic alternative to the treatment of acute cholecystitis in patients that present as prohibitive surgical candidates. Modern percutaneous techniques allow for minimally invasive and accurate placement of these tubes within the lumen of the diseased gallbladder. Following successful placement, the PCT is then used for gallbladder aspiration and drainage, trans-cystic biliary decompression, dilation of biliary strictures, and stenting of the bile ducts.

In the United States, it has been estimated that approximately 10–15% of the adult population have gallstones. Of this cohort, 1–4% will have gallstone-related symptoms manifest as biliary cholic. Among these, 20% will—approximately 400,000 patients—develop acute complications in the form of acute cholecystitis, choledocholithiasis, gallstone pancreatitis, or gallstone ileus [1–4]. Cholecystectomy remains the standard of care for resolution and prevention of recurrence of these complications. The reported incidence of cholecystectomy is broad, from 600,000 to 1.5 million operations per year in the United States. While there is large variability in the numbers quoted, the overwhelming consensus is that gallbladder pathology is pervasive and the need for intervention is common. That said, despite technical advancement in the surgical treatment of gallbladder disease, complications remain an issue. Overall, the reported complication rates range from 1% to 12%, with a 0.02–0.2% risk of common bile duct injury. While these are relatively low numbers, when applied to the large number of procedures per year, these complication rates become a significant factor in ongoing morbidity and increased cost of care.

PCTs have become a safe tool for the management of acute cholecystitis in patients deemed high risk for operative intervention at the time of their diagnosis. The primary factors influencing fitness for operative intervention include acute critical illness, severity of preexisting comorbid conditions, or a known higher risk of surgery specific complications including bile duct injury [5, 6]. With regard to this patient population, the literature governing the selection criteria of those who would most benefit from PCT placement is quite variable. While a general consensus may not exist, the recently updated 2018 Tokyo Guidelines are frequently used to help differentiate which cohort of patients would qualify and benefit from a PCT [7]. These guidelines established a grading system to classify the severity of acute cholecystitis, Table 7.1.

In general, patients presenting with Tokyo Grade I cholecystitis should be offered

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**Table 7.1** Tokyo grading for acute cholecystitis

| Grade | Criteria |
|---|---|
| Mild (grade 1) | Acute cholecystitis that does not meet the criteria for a more severe grade mild gallbladder inflammation, no organ dysfunction |
| Moderate (grade 2) | The presence of one or more of the following:<br>Elevated white-cell count (>18,000 cells per cubic millimeter)<br>Palpable, tender mass in the right upper quadrant<br>Duration >72 h<br>Marked local inflammation including biliary peritonitis, pericholecystic abscess, hepatic abscess, gangrenous cholecystitis, emphysematous cholecystitis |
| Severe (grade 3) | The presence of one or more of the following:<br>Cardiovascular dysfunction (hypotension requiring treatment with dopamine at ≥5 μg per kilogram of body weight per minute or any dose of dobutamine)<br>Neurologic dysfunction (decreased level of consciousness)<br>Respiratory dysfunction (ratio of partial pressure of arterial oxygen to the fraction of inspired oxygen <300)<br>Renal dysfunction (oliguria; creatinine level, >2.0 mg/deciliter)<br>Hepatic dysfunction (prothrombin time—international normalized ratio, >1.5)<br>Hematologic dysfunction (platelet count, <100,000 per cubic millimeter) |

cholecystectomy based on response to initial resuscitation. In patients presenting with Tokyo Grade II cholecystitis, every effort should be made to perform a cholecystectomy within 48 h of presentation. However, if the patient has symptoms for more than 3 days, comorbidities that would preclude the use of general anesthesia, advanced metastatic disease, or other history that would further complicate the cholecystectomy, then a PCT should be considered. This consideration can be based upon and standardized through use and application of empiric scoring systems which include, but are not limited to, the Charlson Comorbidity Index and American Society of Anesthesiologists (ASA) Classification. Use of these tools allow institutional development of treatment protocols based upon an individual patient population. In those patients with Tokyo Grade III cholecystitis, a PCT should be strongly considered unless the patient demonstrates a complete response to resuscitation and is otherwise healthy (Fig. 7.1).

## 7.2 Technique

A PCT is placed under radiologic guidance. Currently, ultrasonography is the most common method used due to its ease of use, portability, and low risk. However, computed tomography (CT) is also frequently used with modern multislice scanners providing a high level of spatial resolution. In contrast to ultrasound machines, CT scanners are more expensive and cumbersome. While this certainly is a factor in modality choice, CT is often more efficacious in those patients where the gallbladder is not easily visualized due to the extent of the acute inflammatory change, body habitus, overlying bowel loops, or other anatomic aberrations (Fig. 7.2).

During placement of a PCT, anesthesia in the form of conscious sedation is administered to the patient. This typically consists of a combination of rapid-onset, short-acting agents that include a narcotic (e.g., fentanyl) for analgesia as well as either a benzodiazepine (e.g., midazolam) or other sedative (e.g., propofol) for anxiolysis and amnesia. Local anesthetic is also frequently used to infiltrate the skin and subcutaneous tissues at the insertion site.

After appropriate level of sedation has been obtained, the Seldinger technique is used to place the PCT. First, an 18–22G needle is used to access the gallbladder. Aspiration of bile (or pus in the case of suppurative cholecystitis) and imaging confirms proper intralumenal placement. The gallbladder aspirate should be sent for microbiologic analysis to include Gram stain, culture, and antibiotic sensitivities. A guidewire is then inserted, and the access needle with-

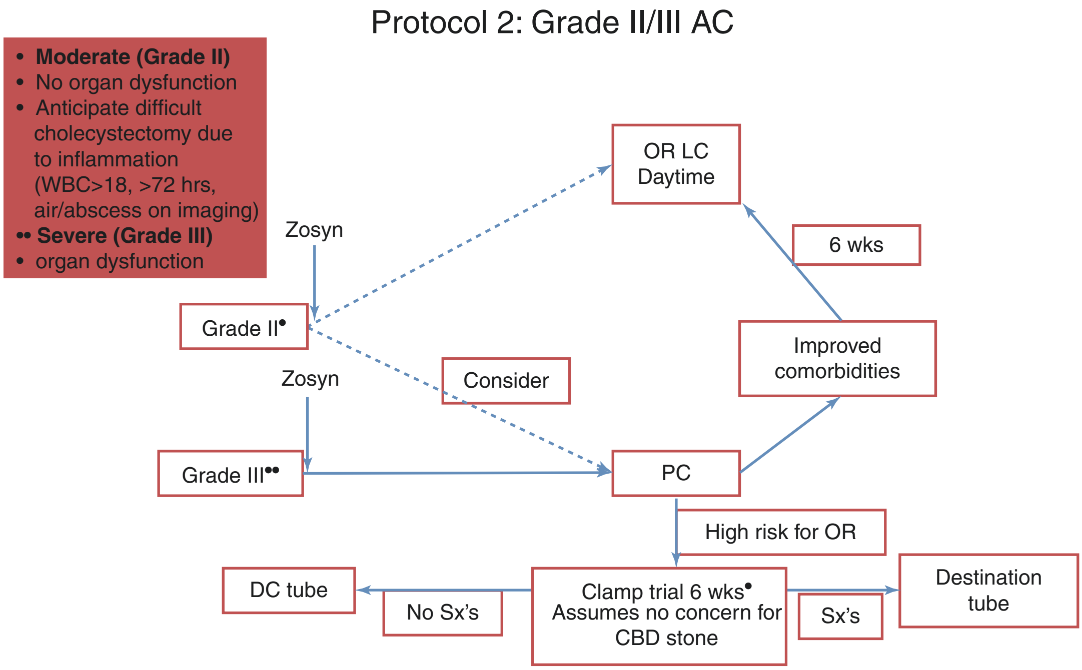



**Fig. 7.1** Grade II/III Acute Cholecystitis Algorithm

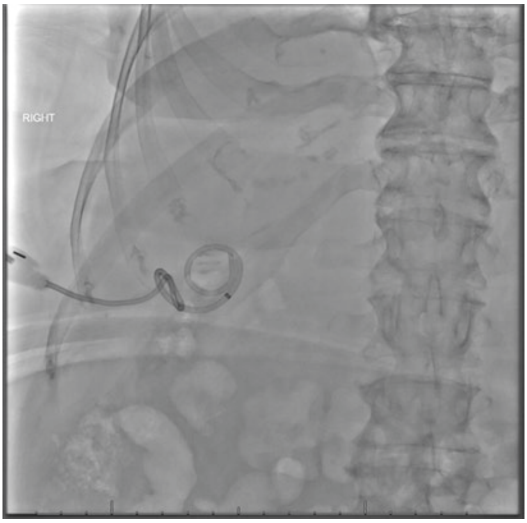
**Fig. 7.2** Computed Tomography Guided Percutaneous Cholecystostomy Tube Placement. 74-year-old female with Tokyo Grade III acute cholecystitis, pancreatitis, septic shock, and hypercarbic respiratory failure

drawn. Then, depending on the type and size of the drain to be placed, the tract may need to be dilated. A drain—typically an 8F or 10F pigtail-type—is then advanced over the guidewire into the gallbladder lumen. Finally, a fluoroscopic cholecystogram is typically obtained to confirm placement, evaluate for cystic duct patency, and delineate the extra-cystic ductal anatomy in the porta hepatis [6] (Figs. 7.3 and 7.4).

## 7.3 Management After Placement

Once the percutaneous cholecystostomy tube (PCT) has been placed, the post-procedural care of the patient is typically managed by the general surgery service. Initial considerations include ensuring source control has been achieved, appropriate resuscitation from the systemic inflammatory response, and treatment of comorbidities. Later, the surgical team will need to determine appropriate discharge disposition and organize close follow-up that will necessarily include ongoing evaluation and management of the PCT, its discontinuation, or planning for interval cholecystectomy.

Intravenous antibiotics started upon diagnosis of acute cholecystitis should be continued.




**Figs. 7.3 and 7.4** Fluoroscopic Cholangiogram via Percutaneous Cholecystostomy. 74-year-old female with Tokyo Grade III acute cholecystitis, pancreatitis, septic shock, and hypercarbic respiratory failure

**Fig. 7.5** Patient with Cholecystostomy Tube in Place

Immediately after successful placement, the patient may clinically worsen. Patients can demonstrate an escalation of the systemic inflammatory response that may be worse than on initial presentation; including fever, diaphoresis, tachycardia, and hypotension, and, in the worst case, evidence of end-organ hypoperfusion leading to organ dysfunction. This response is presumed to be secondary to transient bacteremia and systemic inflammation caused by the drain placement. Appropriate steps are necessarily taken to monitor the patient's hemodynamics based on the degree of their response. Should the patient begin to decompensate, they will likely warrant a higher level of care with advanced therapies. Despite the potential for clinical decline, it is important to note most patients do not have these issues and experience symptomatic relief within 24 h of placement [8] (Fig. 7.5).

Once the patient has demonstrated clinical improvement, the decision must be made regarding the duration of antibiotic therapy. Traditionally, despite little high-quality data to guide decision-making, the duration of antibiotics following PCT has been 7–10 days or upon resolution of symptoms and/or various clinical parameters. However, given continually mounting concerns regarding antibiotic stewardship, the current overall trend in the management of intra-abdominal sepsis has been to decrease the duration of antibiotic therapy. This change in management paradigm was, in part, initiated as a result of the often-quoted Study to Optimize Peritoneal Infection Therapy (STOP-IT) trial. This randomized trial demonstrated the non-inferiority of 4 days of antibiotics compared to 8 days following abdominal surgical source control. It is crucial to note, however, that in this study only 10.8% of those patients had biliary infections. Further, the number treated with cholecystectomy was not reported [9]. That said, several smaller studies have shown the non-inferiority of antibiotic treatment regimens of less than a week in patients treated with PCT [10, 11]. With deference to this trend and the mounting data in support of shorter antibiotic duration, the 2018 Tokyo Guidelines suggest a duration of 4–7 days of antibiotics even for patients with systemic manifestations of cholecystitis (i.e., Grade III) following PCT placement [7].

The antibiotic regimen selected should be guided by the bile culture obtained during PCT placement as well as the local antibiogram. In general, coverage should initially consist of broad-spectrum agents that can be narrowed as dictated by the culture results. In patients with Grade III cholecystitis, an anti-pseudomonal agent is recommended [7]. Of note, there is debate about whether consideration should be given to a more prolonged course should cultures grow Gram positive organisms. In this case, there is conflicting evidence with respect to the optimal duration, with some advocating for 2-week duration. This represents an important exception to the 4- to 7-day paradigm. Finally, antibiotic selection and duration should be discussed with an interdisciplinary team prior to discharge [12]. In our practice, antibiotics are transitioned from IV to oral within 24 h provided the patient demonstrates clinical improvement. Patients are discharged on oral antibiotics for a total course of 4–7 days at the discretion of the attending surgeon.

With resolution of symptoms, a diet can be reintroduced and advanced as tolerated following PCT placement. The patient is appropriate for discharge with resolution of symptoms, normalization of physiology, and intake of adequate enteral nutrition. Clearly, the cohort of patients who receive a PCT will have factors making a routine discharge home not feasible. Each patient will necessarily need individualized case management and coordination, preferably by a multidisciplinary team.

An important consideration is ensuring the PCT is managed properly after discharge. Careful patient education prior to discharge is essential for both the patient and the healthcare system as most reinterventions are due to tube dislodgement [13, 14]. The patient or appropriate caregiver should be educated in how to care for the tube and its external apparatus in order to maintain proper positioning and patency. In addition, they should be instructed in how to record daily outputs as this will help the surgical team with future clinical decision-making.

In our practice, follow up is performed at 2 weeks from discharge from the hospital. An interim history is obtained, and physical exam performed. The drain output record is reviewed. In the event of output greater than 100 ml/day, the PCT is interrogated for distal obstruction via trans-PCT cholangiography. Provided output is less than 100 ml/day and the patient remains asymptomatic, the decision upon whether to perform an interval cholecystectomy or continue nonoperative management with the PCT as destination therapy can then be considered.

## 7.4 Interval Cholecystectomy

At the 2-week follow-up, if the patient has shown improvement and is deemed a potential candidate to proceed with interval cholecystectomy, steps are taken to optimize them for surgery. The primary areas to address include all comorbidities that initially prompted the placement of the PCT. A plan should be established with the patient to optimize their functional status with a specific exercise program. Diet plans and nutrition goals should be discussed. Any specialists or consultants necessary to achieve these goals should be involved.

In our practice, the patient will return for a second follow-up in 4 weeks (6 weeks after PCT placement) to be reevaluated. Should the patient remain a candidate for surgery, elective cholecystectomy can be scheduled at that time. We have shown that tube removal without interval cholecystectomy confers a 10.6% incidence of recurrent cholecystitis, so every effort is made to maintain patency of the tube until operation [13]. Otherwise, the patient will remain in the nonoperative management algorithm. The PCT should remain in place until the time of surgery because of the risk of recurrence [15]. Ultimately, the optimal timing of the surgery varies widely in the surgical literature. However, generally accepted criteria for interval cholecystectomy include complete resolution of symptoms and fitness to undergo general anesthesia. We do not offer the surgery until a minimum of 6 weeks after placement of the PCT but as soon as possible thereafter.

A recent study has shown that younger patients, those with fewer comorbidities, and those presenting with lower APACHE II scores were more likely to progress to interval cholecystectomy. During the postoperative period, 5% of these patients suffered a major postoperative complication with 12% of patients having complication manifest from prior comorbidity [14]. These data are similar to other studies reporting on the total perioperative morbidity for initial cholecystectomy in acute cholecystitis [16]. However, despite these promising statistics, the degree of acute and chronic inflammation may complicate the operation, making the critical view of safety harder to obtain. This subsequent technical difficulty is likely responsible for some studies suggesting a higher rate (10%) of biliary complications in cholecystectomy in patients who had undergone preoperative PCT [17]. While the literature is clear with respect to the benefit of proceeding with interval cholecystectomy in appropriate patients, the increased rate of complications shows the importance of ensuring these operations are under optimal operative conditions.

## 7.5 Nonoperative Management

If a patient presents at the 2-week follow-up and is deemed to have medical conditions precluding them from an interval cholecystectomy, they remain in the nonoperative management algorithm. The primary factor prompting ongoing nonoperative management is continuing medical comorbidities felt to elevate the risks of cholecystectomy beyond the morbidity of the PCT. Disseminated malignancy or a short life expectancy is an additional indication for definitive nonoperative management.

In the case that cholecystectomy is prohibitive, the PCT is then interrogated. If the output is low (less than 100 ml/day), the PCT is clamped. During the trial, patients are instructed to keep the PCT clamped unless they have recurrence of their original symptoms. In this case, they are instructed to unclamp the PCT in order to decompress the biliary system. Patients then return to clinic in 6 weeks with repeat imaging, dedicated right upper quadrant or CT.

While the data suggest decreased complications with PCT, its discontinuation, if appropriate, is seen as preferable with respect to patient comfort, risk of drain-related complication, and burden on the healthcare system [17]. While this is a generally agreed-upon principle, there is no consensus in the current literature on the ideal timing for PCT removal [18]. In our practice, the PCT is removed if the patient continues to have comorbidities or malignancy precluding operative intervention but remains asymptomatic during the subsequent clamp trial. However, patients with residual gallstones have a higher risk for recurrence even if asymptomatic during the 4 weeks of the clamp trial. In this setting, this risk in some studies is as high as 41% [19]. If available, percutaneous gallstone extraction can be offered. Conversely, despite having more comorbidities precluding safe interval cholecystectomy, patients with acalculous cholecystitis have a lower risk for recurrence [20].

If the patient develops recurrent symptoms during the clamp trial, the PCT is left in place and becomes destination therapy. The PCT is then used as needed to decompress the biliary system with the onset of recurrent symptoms. Close follow-up must be maintained to ensure the frequent decompression does not result in depletion of bile salts and subsequent nutritional deficiencies. In our practice, if the PCT is deemed to be destination therapy, care of the patient is transitioned from the general surgery to the interventional radiology service once out of the acute period. The intervention radiologists then maintain the drain with follow-up approximately every 12 weeks for PCT exchange [13].

Finally, an emerging alternative to committing patients to a destination PCT is endoscopic decompression of the gallbladder into the gastrointestinal lumen with self-expanding stent placement. Initial studies have shown a high success rate and comparable outcomes to PCT placement [21, 22]. While the goal of endoscopic decompression is to serve as a temporizing procedure prior to cholecystectomy, chronic inflammation and scar formation may make future operation difficult. Further investigation is needed to determine if endoscopic drainage and stent placement can serve as a stand-alone procedure.

## 7.6 Conclusion

PCT is an appropriate therapy for severe acute cholecystitis (Tokyo Grade III), or acute cholecystitis in patients who are at high risk for general anesthesia and cholecystectomy due to advanced malignancy or medical comorbidities (Tokyo Grade II). After the PCT is placed and the patient recovers from their acute illness, the treatment team will have to decide if the PCT will be a bridge to cholecystectomy or destination therapy. In select patients who are not operative candidates and meet criteria, the PCT may be eventually removed with acceptable rates of recurrence.

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# 8 Difficult Laparoscopic Cholecystectomy: Intraoperative Evaluation

Philip J. Townend, Rupaly Pande, Henry Bergmann, and Ewen A. Griffiths

## 8.1 Introduction

Since the 1990s, laparoscopic cholecystectomy has become the 'gold standard' treatment for gall stone disease [1]. Initially there was some controversy due to a higher reported rate of bile duct injury (BDI) and vasculobiliary injuries (VBI); however, this was principally a learning curve issue, and a large study of over half a million patients over a 30-year period has shown LC has become safer over time. It found that reported rates of BDI have reduced over time (1994–1999: 0.69% (range 0.52–0.84%) versus 2010–2015 0.22% (range 0.02–0.40%); $p = 0.011$) [2]. In addition, there has also been a decrease in conversion to open surgery rates. LC has subsequently been shown to be equally as safe with no increased risk of BDI, shorter hospital stay and decreased overall hospital costs even when some LC has increased operating times [3]. LC is now a very common operation which may vary in operative difficulty. For example, it can be a routine operation comfortably performed by a training grade surgeon (with appropriate supervision) but, at its most difficult, can tax even the most experienced specialist surgeon. The difficult LC is associated with higher operative duration, conversion to open surgery, 30-day complications and 30-day reintervention [4].

The difficult LC can often be predicted based on preoperative evaluation as discussed in previous chapters. The authors of this chapter recommend the use of the choles difficult laparoscopic cholecystectomy score which is preoperative score developed from two large, high-quality prospective series of cholecystectomy patients [5]. The score includes factors which were independently associated with difficulty and included increasing age, ASA score, male gender, diagnosis of CBD stone or cholecystitis, thick-walled gallbladders, CBD dilation, use of preoperative ERCP and non-elective operations. This can allow the surgical team (surgeon, anaesthetist, trainees, theatre staff, etc) to plan for extra theatre time and specialist equipment on standby, if necessary, or refer out to a specialist. There are times however when the operative conditions can come as a surprise, and the surgeon needs to know how to adapt to the hostile operating conditions. These cases can present in both emergency and elective settings.

This chapter will discuss the intraoperative evaluation the surgeon must undertake to tackle

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the difficult gallbladder (GB). We will also discuss some helpful grading systems for standardise assessment and evaluation of difficult cases, safe dissection approaches with respect to key anatomical features and specific operative scenarios which may challenge the surgeon. It must be remembered that the surgeon's primary objective is to avoid BDI and VBI. The secondary objective is to remove the gallbladder. Bail out options to avoid injury to the patient include performing a subtotal cholecystectomy (reconstituting or fenestrated) [6], cholecystostomy drainage tube insertion, open conversion or abandoning the operation entirely and referral to a specialist hepatobiliary surgeon.

## 8.2 Gallbladder Difficulty: Intraoperative Features

Whilst there are a variety of preoperative variables which are reliable predictors of the difficult LC, it is only when the gallbladder and liver are visualised laparoscopically (or not if the adhesions and inflammation are so extensive) that the true nature of how difficult the operation may be becomes apparent. Intraoperative features which are associated with a difficult cholecystectomy are shown in Table 8.1, categorised between those related to the gallbladder and those unrelated to the gallbladder. Very few of these factors are reversible, although it is recognised that there is still a place for delayed cholecystectomy in certain scenarios—that is, when a patient is admitted acutely with cholecystitis and treated conservatively and brought back in for a planned cholecystectomy after around 6–8 weeks of 'cooling' off to allow safe laparoscopic cholecystectomy [7, 8]. Scenarios where this might be appropriate include when the duration of cholecystitis is greater than 7 days (as cholecystectomy can be extremely challenging within this time frame) or when the patient is borderline fit for surgery and requires medical optimisation prior to surgery.

Obesity and non-alcoholic fatty liver disease are known to increase the difficulty of LC (due to access issues and difficultly in retracting the liver due to stiffness) and in the elective setting this should be addressed with appropriate lifestyle advice. A randomised trial of a 2-week very low calorie diet (VLCD) in obese patients has been shown to reduce operating times and make obtaining the critical view easier [9]. The authors of this chapter use this VLCD in patients with known fatty liver or whose BMI is over 35 to make laparoscopic surgery easier. Patients who comply with this VLCD have been shown to have easier operations due to the weight loss and easier retraction of the liver, so explaining the rationale for the diet and its importance is paramount [10]. There are a variety of VLCD plans which include either commercial shakes, calorie counting or a 'milk and yoghurt' diet plan.

**Table 8.1** Intraoperative features that make laparoscopic cholecystectomy more difficult

| Factors related to the gallbladder | Intra-abdominal factors unrelated to the gallbladder |
|---|---|
| Gallbladder adhesions (acute or chronic) | Adhesions (from previous operations) |
| Fibrosis and scarring of the gallbladder | Obesity and excessive visceral fat |
| Fibrosis and scarring of the hepato-cystic triangle | Non-alcoholic fatty liver disease |
| Atrophic or contracted gallbladder | Cirrhotic liver |
| Intrahepatic gallbladder | Biliary anomalies |
| Impacted stone in the neck of the gallbladder | Vascular anomalies |
| Cystic duct and CBD stones | Left-sided gallbladder |
| Gallbladder necrosis | Situs inversus |
| Mirizzi syndrome | Other liver pathology, for example large liver cysts |
| Abscess formation | |
| Perforated gallbladder | |
| Cholecystectomy tube in situ | |
| Cholecystoenteric fistula | |

## 8.3 Intraoperative Gallbladder Difficulty Scores

Being able to stratify intraoperative difficulty with a simple scale of operative difficulty has the advantages of assisting in intraoperative strategy and planning; allowing comparison across different research studies; facilitating risk adjustment for surgical outcomes and providing an aid in training surgeons and monitoring of training progression. Several intraoperative scoring and other scoring systems have developed for the use in cholecystectomy. These include the Nassar scale [4, 11], Cuschieri scale [12], Parkland scale [13, 14], WSES score [15], the American Association for the Surgery of Trauma (AAST) [16] and Tokyo Guidelines Grading for cholecystitis [17] (Tables 8.2 and 8.3). Each of these have different systems of grading the operative difficulty, although broadly similar, and most have been correlated with post-operative outcomes. Only the Nassar score has been validated in two large prospective series of patients and is correlated with worsening outcomes (including operative duration, conversion to open surgery, 30-day mortality and 30-day complications) [4, 11]. In addition, a preoperative risk prediction score is available which correlates with the Nassar score intraoperatively [5]. Whilst the other scores do have utility, the authors would recommend the Nassar scale for these reasons. This simple operative difficulty scale can be used by multiple grades of surgeons (including trainees and consultants) and remain highly clinically relevant. It therefore provides a tool for reporting disease and intraoperative severity and can reliably be utilised in future research to adjust outcomes according to case mix and intraoperative difficulty. It is recommended that grading systems should be routinely used in all cholecystectomies and recorded in the operative report.

## 8.4 General Safe Dissection Approaches

Safe dissection approaches also include calm decision-making during the operation and the ability to adapt and change the operation and 'bail out if necessary' to avoid BDI or VBI (Fig. 8.1). It is important during difficult LC for the surgeon to orientate themselves multiple times during the procedure to important landmarks such as the duodenum, colon, hepatoduodenal ligament, bile duct, hepatic artery, Rouviere's sulcus, segment 4 of the liver and the more recently described R4U line [18]. This is especially true when attempting to dissect out the critical view of safety where risk of BDI is greatest. It has been shown that the most bile duct injuries during LC occur due to misperception of the anatomy as opposed to faults in technical skills or knowledge. An analysis of 252 laparoscopic bile duct injuries showed 97% of cases were due to a visual perception illusion and found only 3% due to faults in technique and skill [19]. We will discuss some useful anatomical landmarks to identify the 'safe' zones and 'danger' zones of dissection and the rationale for using them. We will also discuss the importance of the critical view of safety (CVS) in the difficult LC and the reason why it is preferable but not paramount to achieve in all cases, especially when there are other safer surgical alternatives.

## 8.5 Rouviere's Sulcus

Rouviere's sulcus was originally described by French anatomist Henre Rouviere in 1924, over 60 years before the first laparoscopic cholecystectomy [20]. It is found to the right of the hepatoduodenal ligament, is normally about 2–3 cm long, is anterior to the caudate lobe and usually contains the right portal structures (right portal vein, right hepatic artery and right hepatic duct) [21]. It is found in approximately 80% of patients. When the fundus of the gallbladder is retracted cephalad, the common bile duct will be found below the anterior leaf of the sulcus and the cystic duct and artery will lie above it. In 2002, Hugh developed a surgical checklist that was used for all operations including using Rouviere's sulcus as a reference point and to begin surgical dissection ventral to this [22]. Hugh published on a single surgeon series of 2000 consecutive LCs, which included a supervised environment with trainees performing the operations without a single major bile duct injury.

**Table 8.2** Nassar, Cushieri, Parkland and WSES G10 scores for assessing and scoring intraoperative difficulty scores for cholecystectomy

| Nassar scale [4, 11] | Cuschieri scale [12] | Parkland scale [13, 14] | *WSES G10 score* [15] |
|---|---|---|---|
| **Grade 1:**<br>*Gallbladder*: Floppy, non-adherent<br>*Cystic pedicle*: Thin and clear<br>*Adhesions*: Simple up to the neck/Hartmann's pouch<br>**Grade 2:**<br>*Gallbladder*: Mucocele, packed with stones<br>*Cystic pedicle*: Fat laden<br>*Adhesions*: Simple up to the body<br>**Grade 3:**<br>*Gallbladder*: Deep fossa, acute cholecystitis, contracted, fibrosis, Hartmann's pouch adherent to CBD, impaction<br>*Cystic pedicle*: Abnormal anatomy or cystic duct—Short, dilated or obscured<br>*Adhesions*: Dense up to fundus; involving hepatic flexure or duodenum<br>**Grade 4:**<br>*Gallbladder*: Completely obscured, empyema, gangrene, mass<br>*Cystic pedicle*: Impossible to clarify<br>*Adhesions*: Dense, fibrosis, wrapping the gallbladder, duodenum or hepatic flexure difficult to separate | **Grade 1:** Easy/uncomplicated cholecystectomy<br>**Grade 2:** Medium difficulty, for example mild cholecystitis, cystic duct or artery obscured by adhesions or fatty tissue; mucocele may be present<br>**Grade 3:** Difficult cholecystectomy due to either gangrenous cholecystitis; shrunken fibrotic gallbladder; severe cholecystitis; subhepatic abscess formation; Hartmann's pouch adherent to the CHD; cases in which the cystic duct or artery are difficult or impossible to dissect or liver cirrhosis with portal hypertension<br>**Grade 4:** Conversion to open surgery is required | **Grade 1:** Normal gallbladder/no adhesions<br>**Grade 2:** Minor adhesions at the neck<br>**Grade 3:** Presence of ANY of the following: Hyperaemia, pericholecystic fluid, adhesions to the body, distended gallbladder<br>**Grade 4:** Presence of ANY of the following: Adhesions obscuring majority of gallbladder or grade I–III with abnormal liver anatomy, intrahepatic gallbladder or impacted stone (Mirizzi)<br>**Grade 5:** Presence of ANY of the following: Perforation, necrosis, inability to visualise the gallbladder due to adhesions | **Gallbladder appearance**<br>Adhesions <50% of GB (1 point)<br>Adhesions burying GB (3 points)<br>**Distension/contraction**<br>Distended GB (or contracted shrivelled GB) (1 point)<br>Unable to grasp with atraumatic laparoscopic forceps (1 point)<br>Stone ≥1 cm impacted in Hartmann's pouch (1 point)<br>**Access**<br>BMI >30 (1 point)<br>Adhesions from previous surgery limiting access (1 point)<br>**Severe sepsis/complications**<br>Bile or pus outside GB (1 point)<br>Time to identify cystic artery and duct >90 min (1 point)<br>**Difficulty**<br>(A) Mild <2<br>(B) Moderate = 2–4<br>(C) Severe = 5–7<br>(D) Extreme = 8–10 |
| **Correlation with outcome data available?**<br>Yes; outcome reports from a prospective single surgeon series of 4089 patients and validation in a large multicentre prospective cohort of 8820. Increasingly difficulty associated with worse clinical outcomes including 30-day complications, reintervention, length of stay and conversion to open surgery. Independent on multivariate analysis | **Correlation with outcome data available?**<br>**No** | **Correlation with outcome data available?**<br>Outcome data available for 50 patients showing increasing severity was associated with longer operating times, length of stay and post-operative bile leaks | **Correlation with outcome data available?**<br>Conversion occurred in 33% of patients with G10 scores of ≥5 in a prospective multicentre study of 504 patients |

**Table 8.3** The American Association for the Surgery of Trauma (AAST) grading of Cholecystectomy Difficulty and the 2018 Tokyo Guidelines. Grading for cholecystitis

| American Association for the Surgery of Trauma (AAST) grading of cholecystectomy difficulty [16, 31] | 2018 Tokyo Guidelines Grading for cholecystitis [16, 17] |
|---|---|
| **Grade 1** is acute cholecystitis<br>**Grade 2** is gangrenous or emphysematous cholecystitis<br>**Grade 3** is localised perforation<br>**Grade 4** is GB perforation with pericholecystic abscess or gastrointestinal fistula<br>**Grade 5** is GB perforation with generalised peritonitis | **Grade I**: Acute cholecystitis does not meet the criteria of "Grade III" or "Grade II" acute cholecystitis. It can also be defined as acute cholecystitis in a healthy patient with no organ dysfunction and mild inflammatory changes in the gallbladder, making cholecystectomy a safe and low-risk operative procedure<br>**Grade II**: Acute cholecystitis is associated with any one of the following conditions:<br>1. Elevated WBC count (>18,000/mm$^3$)<br>2. Palpable tender mass in the right upper abdominal quadrant<br>3. Duration of complaints >72 h<br>4. Marked local inflammation (gangrenous cholecystitis, pericholecystic abscess, hepatic abscess, biliary peritonitis, emphysematous cholecystitis)<br>**Grade III**: Acute cholecystitis is associated with dysfunction of any one of the following organs/systems:<br>1. Cardiovascular dysfunction: Hypotension requiring treatment with dopamine ≥5 μg/kg per min, or any dose of norepinephrine<br>2. Neurological dysfunction: Decreased level of consciousness<br>3. Respiratory dysfunction: PaO2/FiO2 ratio < 300<br>4. Renal dysfunction: Oliguria, creatinine >2.0 mg/dl<br>5. Hepatic dysfunction: PT-INR >1.5<br>6. Haematological dysfunction: Platelet count <100,000/mm$^3$ |
| **Correlation with outcome data available?**<br>Incidence of complications, LOS, ICU use and any adverse event increased with increasing anatomic grade when assessed in a retrospective cohort of 315 patients [16] | **Correlation with outcome data available?**<br>Whilst the 2018 Tokyo guidelines for grading the severity of cholecystitis are based on a combination of laboratory and clinical features as well as intraoperative findings, multiple studies have associated increasing grades of cholecystitis to be associated with length of stay, conversion to open surgery, 30-day mortality and post-operative complications [17] |

## 8.6 R4U Line

The 'R4U line' is a more recently described term that builds on the anatomical principals behind the dissection rules developed, starting dissection above Rouviere's sulcus (Fig. 8.2). It involves an imaginary line from Rouviere's sulcus to the base of segment 4 towards the umbilical fissure [18]. The base of segment 4 often forms a ledge over the left portal pedicle and extends to the left to end at the umbilical fissure. Above the R4U line is the safe zone of dissection containing the gallbladder, cystic duct and cystic artery. Below the R4U line is the 'danger zone' of dissection and contains the common bile duct, hepatic artery and portal vein. In the absence of Rouviere's sulcus, it can still be used as a reference point and give the surgeon an idea of where Rouviere's sulcus should be if it were present.

## 8.7 Critical View of Safety

When LC was introduced as an alternative to open cholecystectomy, there was an increase incidence of bile duct injuries [23]. The most common cause of bile duct injury or 'classic injury' being mistaking the CBD or aberrant right hepatic duct to be the cystic duct [24]. Strasberg et al. described the critical view of

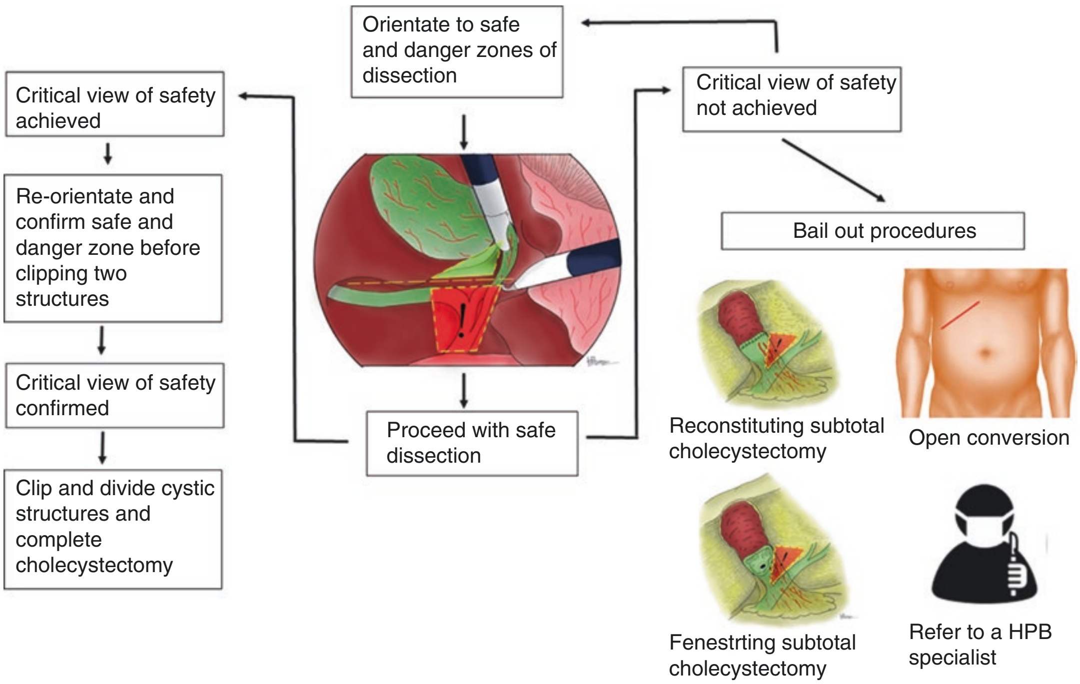


**Fig. 8.1** Algorithm for safe dissection in the difficult laparoscopic cholecystectomy and appropriate bail out options should the critical view of safety not be achieved. The zone of safe dissection is shown with the danger zone. (Courtesy of H. Bergmann)

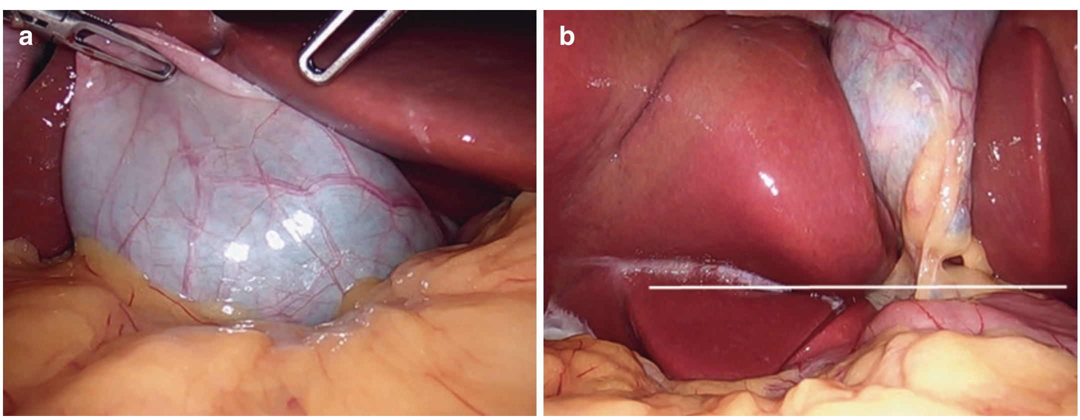


**Fig. 8.2** (**a**)—Nassar Grade 1 cholecystectomy with a thin walled gallbladder and no inflammation or adhesions. (**b**)—Zone of safe dissection in laparoscopic cholecystectomy with the R4U line shown

safety (CVS) and how it should be achieved prior to clipping and dividing any ductal structure so to avoid BDI [25]. The CVS has three components:

1. The fibrous and fatty tissue is dissected off the hepatocystic (HC) triangle.
2. At least one-third of the gallbladder dissected from the gallbladder fossa/cystic plate.
3. Only two structures (cystic artery and cystic duct) are seen entering the gallbladder.

Using this method of dissection allows the surgeon to stay high and away from the cystic duct–

CBD junction and thus reducing the risk of BDI. Only once the CVS is achieved can the surgeon confidently identify the cystic duct and artery, prior to clipping and dividing them. The end result of CVS dissection is seeing the two structures entering the gallbladder and having a third of the gallbladder dissected free to avoid the risk of injuring a looping CBD. Most surgeons attempt to dissect out the HC triangle prior to taking the gallbladder off the cystic plate, particularly in the elective cases. However, in the setting of a difficult LC, sometimes the safer option will be to start dissecting the gallbladder off the liver half way up and creating a tunnel. This often allows better lateral retraction of the gallbladder and makes it safer and easier to dissect out the HC triangle and eventually achieve a critical view.

## 8.8 Specific Scenarios Which Make Cholecystectomy Difficult

### 8.8.1 Biliary and Vascular Anomalies

There are a wide variety of biliary and vascular anomalies which might make laparoscopic cholecystectomy more difficult.

The common biliary anomalies are illustrated in Fig. 8.3. Luckily, because current methods of teaching advocate high dissection and avoid precise identification of the common bile duct and biliary tree, lots of these anomalies go unnoticed by the surgeon. Those of particular note include where the cystic duct is either absent or fibrosed to the CBD as this makes operating hazardous. A wide cystic duct poses a challenge for safe ligation and in this case, when it is confirmed to be the cystic duct, either by the critical view or by intraoperative cholangiogram, ligation can be either with a large Hemolock clip or by suture ligation with an intra-corporeal knot or an endoloop (Fig. 8.4). It is worthy of note that a cystic duct which is larger than a standard clip should be suspected to be the CBD until proven otherwise. Accessory right hepatic ducts can be injured as they can be superficial and lie close to the gallbladder bed, and the management of these is out with the scope of this chapter. However, if any significant biliary abnormality is seen at cholecystectomy and the critical view is in doubt, an intraoperative cholangiogram is recommended.

The cystic artery is usually a single branch of the right hepatic artery in 80% of cases. Vascular anomalies of the cystic artery include the cystic artery passing anterior to the common hepatic/bile duct (17.9%); a short (<1 cm) cystic artery (9.5%); multiple cystic arteries (8.9%) or the cystic artery located inferior to the cystic duct (4.9%).

Anomalies of the right hepatic artery (RHA) are common and can make cholecystectomy difficult. A replaced RHA may be confused as the cystic artery and inadvertently ligated during cholecystectomy; if this is also associated with a CBD injury this has a poor prognosis as a simple biliary reconstruction may not be possible and a liver resection and more complex reconstruction may be required.

## 8.9 Acute Cholecystitis

When acute cholecystitis is present and an obstructing stone is found in the cystic duct or Hartmann's pouch, the gallbladder can be extremely distended (Fig. 8.5a). In this scenario, the gallbladder should be aspirated to allow grasping and retraction (Fig. 8.5b). Inflammatory adhesions are best dealt with a combination of blunt and sharp dissection (Fig. 8.5c). The surgeon should be cognisant of the risk of injury to the duodenum or transverse colon which can be stuck and fibrosed to the gallbladder in this area. This scenario is likely if the cholecystitis is advanced and has been going on for many days (>7 days) or if a fistula is present. Necrotising cholecystitis with gallbladder wall necrosis (Fig. 8.5d) is usually easy to separate from the liver if the correct plane is entered. However, as these operations are usually more bloody and have a risk of post-operative collections or bile leaks the surgeon should consider the need to place an abdominal drain at the conclusion of surgery.

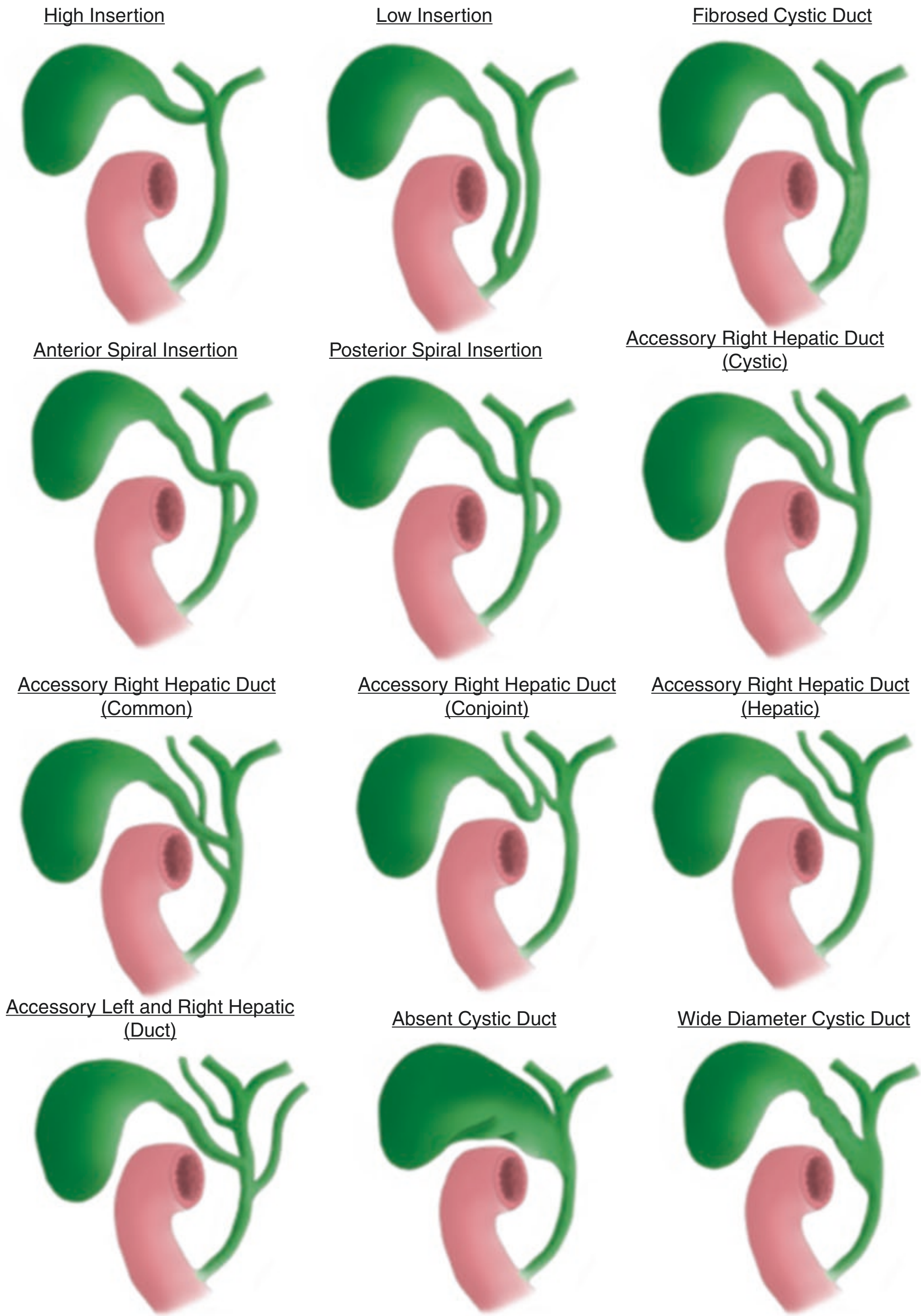


**Fig. 8.3** Common biliary tract anomalies relevant to difficult cholecystectomy. (Courtesy of H. Bergmann)

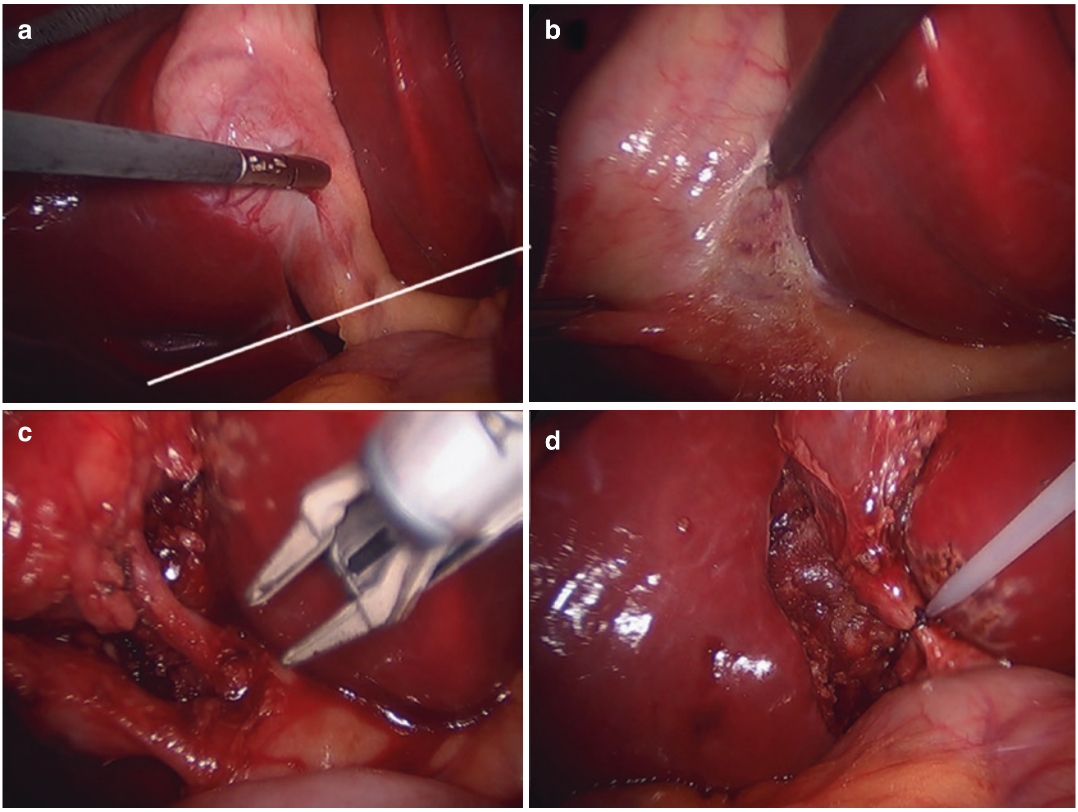


**Fig. 8.4** (**a**)—R4U line drawn before dissection in a mildly inflamed gallbladder. (**b**)—Initial peritoneal dissection. (**c**)—Critical view of safety with the cystic artery about to be divided. (**d**)—The wide cystic duct was ligated by the use of an endoloop technique

## 8.10 Acute on Chronic Cholecystitis

Patients with a more chronic history can present with adhesions to the omentum and liver which are more fibrotic than inflammatory (Fig. 8.6a). This patient had a history of gallstones going back many years and the omentum had walled off the gallbladder almost completely. They presented with an acute attack of cholecystitis (acute on chronic cholecystitis). With careful laparoscopic dissection adhering to the rules set out above the critical view of safety was achieved (Fig. 8.6b).

## 8.11 Previous Cholecystostomy Drainage Tube

Radiological percutaneous cholecystostomy tubes have been increasingly used in the treatment of patients with severe acute cholecystitis, especially if the patient is unfit for surgery and not responding to non-operative treatment with intravenous antibiotics. These tubes are usually placed transhepatically by a radiologist to avoid the risk of bile leakage on drain removal. The drainage tube resolves the local and systemic sepsis and avoids the risks of emergency surgery. Some patients

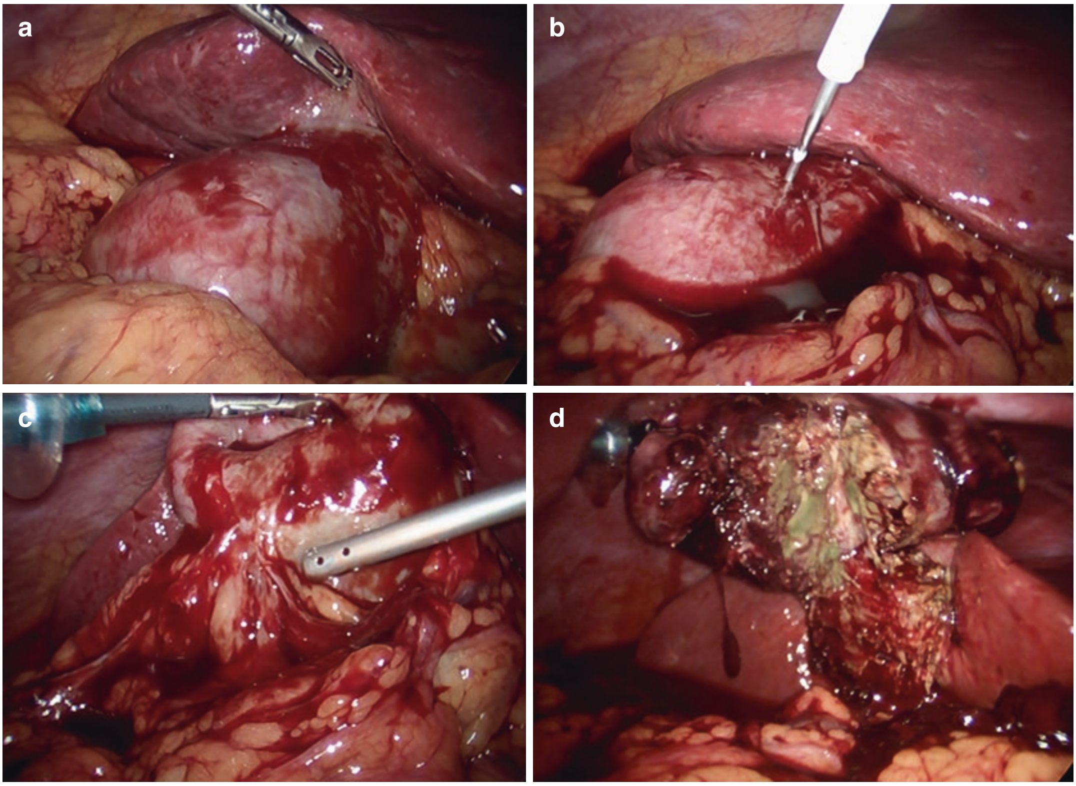

**Fig. 8.5** (**a**)—A tense and distended gallbladder with severe acute cholecystitis present. (**b**)—The gallbladder is aspirated with a long aspiration needle to allow grasping and retraction. (**c**)—The inflammatory adhesions can be tackled with a combination of blunt and sharp dissection. (**d**)—Dissection of the liver reveals the necrotic gallbladder wall

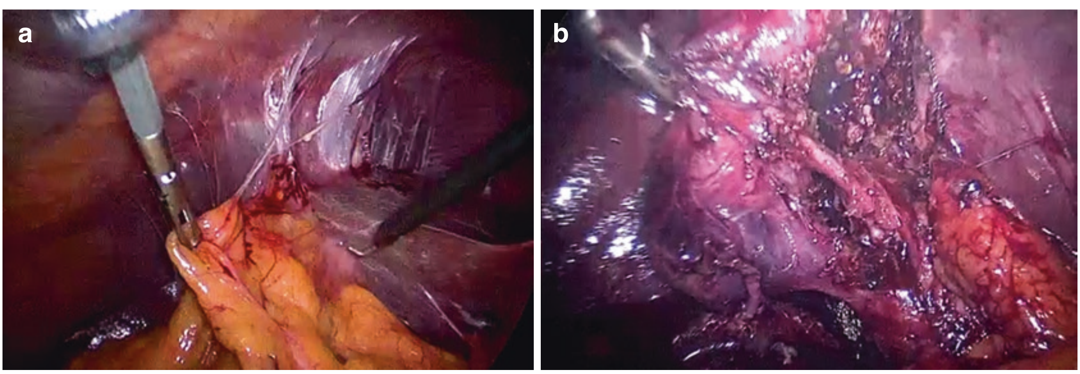

**Fig. 8.6** (**a**)—Features of hepatic and omental adhesions in a patient presenting with acute on chronic cholecystitis. (**b**)—The critical view of safety has been achieved in this difficult cholecystectomy

with reversible pathology (for example myocardial infarction or pneumonia) will subsequently become fit for surgery. They will need careful assessment and pre-optimisation with an anaesthetist and other specialists. However, it is worth mentioning that in a randomised trial of 142 high-risk patients with acute cholecystitis randomised to either cholecystostomy (68 patients) or laparo-

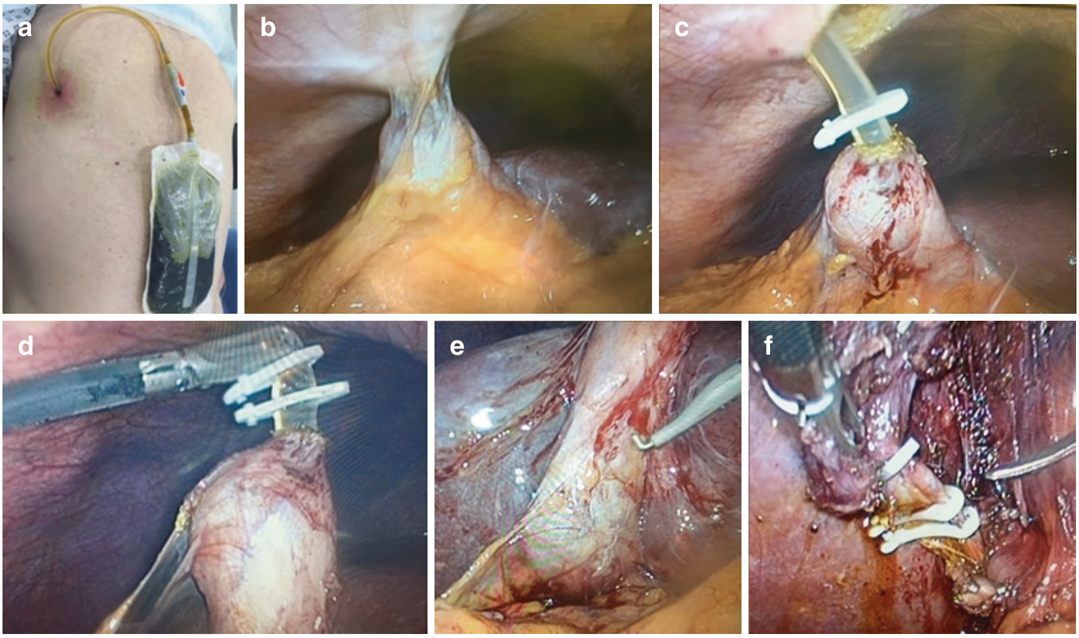


**Fig. 8.7** (**a**)—External view of the draining cholecystostomy tube placed during a 'bail out procedure'. (**b**)—Fibrosis around the Foley catheter tube. (**c**)—The Foley catheter has been clipped to avoid bile leakage, so that the balloon did not deflate. (**d**)—The Foley catheter can be used to manipulate the gallbladder to aid in manipulation of the gallbladder and dissection. (**e**)—Features of chronic cholecystitis. (**f**)—Clipping of the wide cystic duct with Haemolock clips

scopic cholecystectomy (66 patients), surgery was clearly superior in that major complications, and need for reintervention, length of stay and hospital costs were reduced [26]. Therefore, it should be noted that cholecystostomy drainage is only a temporising measure and that surgeons should be involved in the assessment of these patients during the acute admission for consideration of definitive surgery.

In our unit, if the patient is fit for future surgery, we prefer to leave the cholecystostomy tube in situ and then discharge the patient for a delayed cholecystectomy. Extra time should be permitted for the surgery as it is often difficult with fibrosed tissue planes. Before performing surgery, it is wise to perform a cholangiogram via the cholecystostomy catheter to assess for CBD stones and unobstructed passage of contrast to the duodenum.

Figure 8.7a shows the external view of a patient who had a bail out cholecystostomy performed at another unit. In this patient, severe cholecystitis was observed at his initial operation and the surgeon decided to place a Foley catheter as a cholecystostomy drainage tube, rather than risk a very difficult cholecystectomy. After around 3 months of 'cooling' off, he underwent a laparoscopic cholecystectomy in our unit. Figure 8.7b shows fibrosis around the tube. The Foley catheter was clipped with a Hemolock clip to allow the balloon to remain inflated and avoid bile spillage (Fig. 8.7c). This allowed the cut Foley catheter to be grasped and manipulate the gallbladder to aid in the dissection (Fig. 8.7d). In this operation, difficult tissue planes are observed (Fig. 8.7e), but the operation is completed laparoscopically with the critical view of safety achieved and the cystic duct divided with Hemolock clips.

## 8.12 Suspected Gallbladder Cancer

The occurrence of incidental gallbladder cancer found at laparoscopic cholecystectomy in around 0.19% to 2.8% of cases depending on the published series [27]. The disease is rare in Europe and is more common in Chile, Japan and North India [27]. Only around 30% of gallbladder cancers are suspected preoperatively; patients at risk include patients with suspicious imaging features (focal GB wall thickening, intra-mural nodules, halo sign, intrahepatic duct dilation or loss of interface between the gallbladder and liver, enlarging ‘polyps’, a porcelain gallbladder, CT imaging showing liver invasion or incidental PET positive gallbladder lesions) or other features such as advanced age, weight loss or raised alkaline phosphatase. Some patients are only diagnosed on subsequent histopathological examination of the gallbladder specimen after the gallbladder is removed at laparoscopic cholecystectomy. Features of gallbladder cancer at laparoscopic cholecystectomy include the abnormal thickening of the gallbladder, peritoneal disease or liver metastases (Fig. 8.8). Some surgeons recommend intraoperative frozen section pathology to diagnose gallbladder cancer with a view to immediate open radical resection (wedge resection of the gallbladder bed and lymphadenectomy). However, we would recommend consulting with a specialist HPB surgeon, aborting the procedure (as the patient is usually not consented for radical liver resection) and performing appropriate staging investigations (spiral CT of the chest and abdomen with IV portovenous contrast) with subsequent HPB MDT/tumour board discussion.

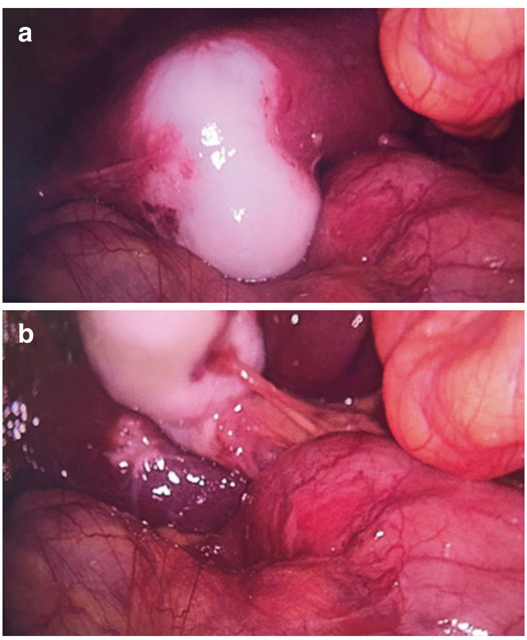


**Fig. 8.8** (**a**) Incidental gallbladder cancer at laparoscopic cholecystectomy with abnormal thickening (**b**) Associated liver metastasis

## 8.13 Xanthogranulomatous Cholecystitis

Xanthogranulomatous cholecystitis (XGC) is often mistaken for, and may predispose to, gallbladder carcinoma [28]. It is usually a histological diagnosis and can be diagnosed on preoperative FNA sampling of the gallbladder via endoscopic ultrasound or on frozen section histology at surgery. Focal GB wall thickening favours gallbladder cancer whilst diffuse thickening favours XGC. The condition is associated with hostile operating conditions and a difficult cholecystectomy as the rates of inflammatory adhesions, fistulae to adjacent organs and post-operative infection rates are higher than a normal cholecystectomy as this reflects the chronic inflammatory nature of this condition. The disease has a high risk of conversions to open surgery for these reasons.

## 8.14 Mirizzi Syndrome

Mirizzi syndrome is a complication of long-standing cholelithiasis and makes cholecystectomy extremely challenging with a significant increase in the risk of intraoperative biliary injury [29]. It may only become apparent at operative surgery and poses particular risk to the surgeon and patients.

Mirizzi syndrome is subclassified in to five types [30]:

- Type 1: is obstruction of the extrahepatic bile duct by stone/s in the Hartmann’s pouch or cystic duct.

- Type 2: is with a cholecystocholedochal fistula (diameter < 1/3 or the common hepatic duct wall).
- Type 3: is with a cholecystocholedochal fistula (diameter < 2/3 of the common hepatic duct wall).
- Type 4: is with a cholecystocholedochal fistula (involving the whole common hepatic duct wall).
- Type 5: any type associated with a cholecystoenteral fistula (i.e. fistula to stomach, duodenum or hepatic flexure or transverse colon). This is sometimes sub-classified depending on whether gallstone ileus is present or not.

This modified Csendes classification is shown in Fig. 8.9**.**

The classic presentation of Type 1 Mirizzi is painless obstructive jaundice with evidence, at ultrasonography, of a gallstone impacted in the gallbladder infundibulum and obstruction of the CBD with consequent dilation of the intrahepatic biliary tree. ERCP and stent insertion may temporise the jaundice and also provide a landmark for protection of the CBD at surgery. Stent insertion will also reduce the risk of bile leakage after surgery.

Mirizzi syndrome can also cause a stricture which mimics biliary cancer. This occurs when the associated inflammatory process is predominant, and it involves the CBD and presents like a malignant stricture. CT, MRCP or ERCP may help differentiate the causes and guide appropriate referral and treatment.

Features of Mirizzi syndrome at surgery include an oedematous or atrophic gallbladder with distortion of Calot's triangle, an impacted gallstone in the infundibulum or the neck of the cystic duct or Hartmann's pouch, thick fibrosis around Calot's triangle, and adhesions under the liver space. Cholecystobiliary fistula should be suspected if the extraction of an impacted stone is followed by the leakage of bile from the common hepatic or common bile duct.

The surgical management of Mirizzi syndrome is outside the scope of this chapter, but can include removal of the gallbladder leaving in place the portion of the infundibulum adherent to the CBD or subtotal cholecystectomy (Type 1 Mirizzi) or cholecystectomy and T-tube insertion

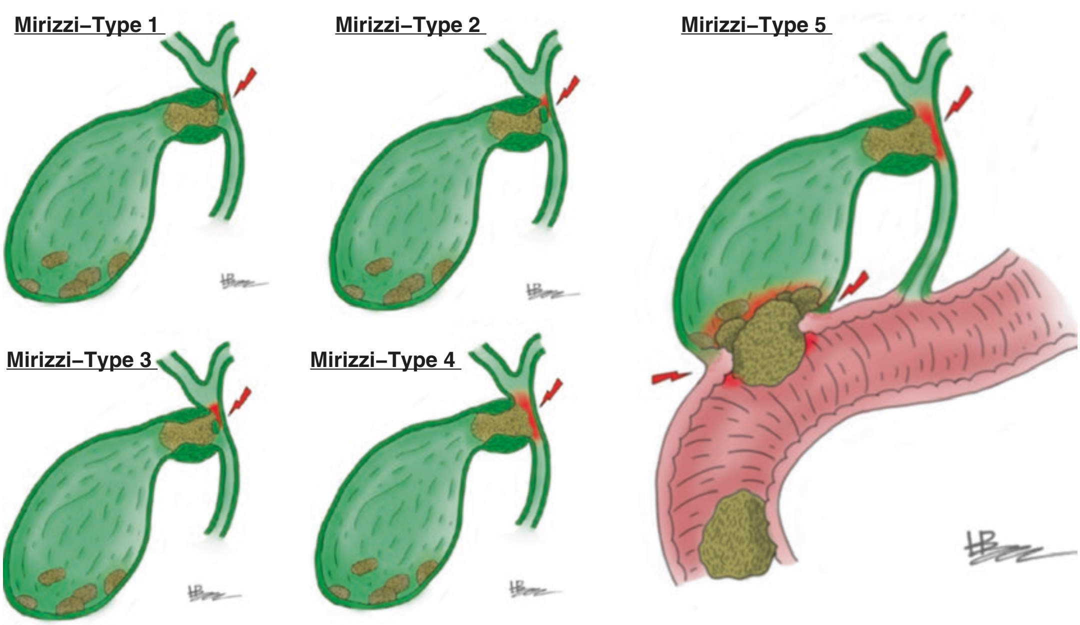


**Fig. 8.9** Modified Csendes classification of Mirizzi syndrome. (Courtesy of H. Bergmann)

or bailing out of the cholecystectomy completely or techniques to resect gallbladder and reconstruct the biliary tree. The decision-making process will depend not only on the fitness of the patient, the condition of the gallbladder and type of Mirizzi but also on the level of skill and expertise of the surgeon. It is strongly recommended that involvement of a specialist HPB surgeon is obtained in these difficult cases.

## 8.15 Summary and Conclusion

Laparoscopic cholecystectomy can be an extremely challenging operation if operative conditions are hazardous. It is important that the surgeons try to predict the difficult case preoperatively (1) to allow extra operative time for the case, (2) consent the patient appropriately and (3) obtain specialist equipement or specialist help with the procedure. We would recommend routinely using one of the Operative Difficultly Scores, such as a the Nassar score for the documentation of operation difficulty. This will allow standardisation, and it will be helpful as a training tool and for surgical audit or morbidity discussions. We hope that this chapter has demonstrated various tips and tricks for dealing with some specific operative scenarios in the difficult case. The surgeon should have a vast array of techniques to use to safely deal with the difficult case, including using techniques to obtain the critical view, performing a subtotal cholecystectomy, placing a cholecystostomy drainage tube or converting to open surgery.

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# 9 Difficult Laparoscopic Cholecystectomy: Timing for Conversion

Samer AlMasri and Ali Hallal

## 9.1 Introduction

Cholelithiasis-related disease is a major cause of global morbidity with its prevalence varying based on several racial, ethnic, and geographical parameters. The disease is three to four times more prevalent in females, and its incidence increases with advancing age in both genders [1]. In the United States (US), 10–15% of the adult population have gallstone, yet more than 80% will remain asymptomatic [2, 3] However, gallstone-related disease constitutes approximately 2.2 million of all annual ambulatory care visits and represents an annual consumption of approximately $6.5 billion, creating a significant health burden in developed countries [3]. On the other hand, the incidence of gallstone-related disease is increasing worldwide in developing countries. This coincides with increase in calorie and fat consumption and sedentary lifestyles in these populations [4]

Laparoscopic cholecystectomy (LC) is the gold standard treatment for benign gallbladder disease and with the growing experience and advanced technical skills, the aforementioned procedure is one of the most commonly performed minimally invasive operation worldwide [5, 6]. Since its was first introduced in the mid-1980s, it has gained widespread popularity because of its advantages that clearly outweigh the open technique. LC is associated with less postoperative pain, shorter length of hospital stay, earlier return to work, and better cosmetic results [7–9]. This in turn leads to a dramatic shift in the surgical management of benign gallbladder disease. Consequently, an expanding number of reports demonstrated the safety and feasibility of this approach for the management of acute cholecystitis (AC) and other gallstone-related complications [5, 7–11].

When performed by well-trained surgeons, LC is an easily reproducible surgical approach that is safe and is associated with a minimal risk of major complications (<5%) [11]. However, there are several patient-related, disease-related, and even surgeon-related variables that can hinder the standard operative steps and increase operative morbidity. Insertion of a cholecystostomy tube, subtotal cholecystectomy, and conversion to the open approach (LOC) are all valid emergency alternatives. LOC, given that the operating surgeon is well familiar with the open approach, promises increased visibility and maneuverability that might aid in the safe removal of the gallbladder. Numerous prior studies have analyzed the incidence of LOC among various patient

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groups and the factors that would increase this risk. Underlying pathology, timing of cholecystectomy, distorted anatomy, adhesions, patients age, body mass index (BMI), gender, comorbidities, and surgeon experience in minimally invasive surgery (MIS) have all been shown to increase the risk of LOC [12–18].

In this chapter, we will be discussing the variables that have been shown to consistently increase the risk of LOC. Furthermore, we will analyze the previously published prediction models and risk scores that help in preoperative surgical planning and patient counseling. Our aim is to highlight the importance of when and why should this approach be considered as a valuable "bailout" technique based on an intraoperative decision rather than a failure on the surgeon's part. This mandate balancing the risk of continuing with the laparoscopic approach with the morbidity associated with LOC.

## 9.2 Risk Factors for Conversion

Preoperative recognition of the risk factors that can hinder a safe LC is crucial, as it increases surgeon awareness and therefore aids in proper patient counseling, guide operative planning, and ultimately optimize patient outcomes. Table 9.1 demonstrates the most commonly cited variables that have been shown to impact the risk of conversion. However, due to the prior significant clinical and methodological heterogeneity in published literature, several of these parameters have either been supported or refuted. Furthermore, there is a wide variation in the actual percentage of conversion reported across various institution that can be as low as 1% [16] or be as high as 32% [19]. This wide variation in the reported conversion rate is related to surgeon experience, patient selection, and procedure-related factors among various studies. Certainly, the conversion rate is decreasing compared to historical figures owing to better preoperative assessment, alternative treatment modalities availability, and enhanced overall surgeon experience. Nevertheless, we will be reviewing the variables that have been consistently proven to impact the risk of conversion across various settings.

**Table 9.1** Risk factors for conversion (CBD: common bile duct)

| |
|---|
| *Patient-related factors* |
| Advanced age |
| Male gender |
| History of multiple upper abdominal operations |
| Obesity |
| Medical comorbidities |
| *Disease-related factors* |
| Acute cholecystitis |
| Gallbladder perforation |
| Gangrenous cholecystitis |
| Gallbladder empyema |
| Emphysematous cholecystitis |
| Imaging parameters (gallbladder wall thickness, pericholecystic fluid, CBD size) |
| Mirizzi syndrome |
| Gallstone pancreatitis and coledocholithiasis |
| Chronic cholecystitis |
| Minimally invasive surgical training (MIST) |

### 9.2.1 Patient-Related Factors

#### 9.2.1.1 Age and Gender

Male gender and advanced age (particularly <65) are two of the most commonly cited variables that have been shown to increase the risk of LOC across multiple prior systematic reviews, meta-analysis, prospective, and retrospective studies [12, 13, 15–21] It has been postulated that male gender is associated with increased severity of the underlying inflammatory process that would hinder safe dissection of the triangle of Calot and increase the risk of conversion [21, 22]. On the other hand, the increased risk of LOC seen in the elderly population can be explained by the fact that in this subcategory of patients, the underlying inflammatory process is more severe. In addition, an elderly patient may have had repeated prior attacks of biliary colic or untreated AC episodes. These variables may lead to the formation of dense adhesions and create anatomical hurdles that would hinder safe dissection during LC and ultimately drive the operating surgeon to abort the LC and convert to open [16, 23, 24].

#### 9.2.1.2 Previous Abdominal Surgery

A history of prior abdominal operations is not a contraindication for LC. However, several studies have shown an increased risk of LOC in the setting of prior abdominal surgeries, particularly those that involve the upper abdomen [16, 25–27]. In a large single-center retrospective review of 4668 LC cases, AlMasri et al. (2018) [16] found that a history of prior abdominal surgeries, especially in the setting of a prior laparotomy for penetrating abdominal trauma, is a strong independent predictor of LOC (OR 4.66, $P = 0.002$). This translates to an increased formation of dense adhesions that obscure safe access and exposure to the hepatocystic triangle, increase the risk of bleeding, iatrogenic injury, and ultimately LOC.

Nevertheless, neither should the nature nor the number of prior abdominal operations preclude the laparoscopic approach. The laparoscopic approach should be the first therapeutic option in symptomatic gallbladder disease as long as the initial access to the abdominal cavity is performed safely and adhesiolysis carried out meticulously until the right upper quadrant is clearly delineated [27].

#### 9.2.1.3 Obesity

Patients with an increased body mass index (BMI) have been reported to be prone to severe underlying inflammation of the gallbladder, making dissection in LC more difficult [24]. More importantly, obesity poses unique technical challenges for the operating surgeon secondary to trocar placement, obscured anatomy secondary to excess intraperitoneal fat, and even an inability to retract the liver sufficiently for adequate exposure [28]. However, while several prior studies have reported obesity (BMI ≥ 30 kg/m$^2$) to be associated with an increased risk of conversion [13, 19, 29], others found no such association [12, 14–16, 20, 28], and the authors concluded that the previously reported increased conversion rate observed in obese patients is attributable to surgeon experience and technical limitations eventually abolishing obesity as a risk factor for LOC. Currently, several reports propose techniques for safe initial trocar placement in the morbidly obese patient for a safe laparoscopic operation [30, 31].

#### 9.2.1.4 Medical Comorbidities

**Cardiopulmonary Disease**

It is well established that the risk LOC is increased in patients with several medical comorbidities. Some of these are specific to LC and others can affect the risk of any laparoscopic procedure. It is believed that patients with cardiopulmonary disease are particularly susceptible to the hemodynamic changes that result from pneumoperitoneal insufflation pressures, as the increase in abdominal pressure is associated with an increase in peak airway pressures, a drop-in stroke volume, and therefore cardiac index [32]. This results in an increased risk of LOC due to the inherent risks that are associated with the laparoscopic approach.

In a large retrospective study involving 20,307 patients from the Danish cholecystectomy database, Harboe and Bardram (2011) [33] found that risk of conversion doubled for patients with American Society of Anesthesiology (ASA) score > 3 compared to patients with a lower ASA score. Furthermore, analysis of prospectively collected data from the National Surgical Quality Improvement Program (NSQIP) by Kaafarani et al. (2010) [34] identified 11,669 patient who underwent cholecystectomy at 117 VA hospitals. They found that patients with more cardiac, pulmonary, renal, and nutritional comorbidities, as reflected by a higher ASA class, had a higher incidence of conversion ($P < 0.05$). The aforementioned variables were also found to be more prevalent in patients who underwent OC from the start.

Finally, in a single institution retrospective study conducted by AlMasri et al. (2018) [16] that aimed to analyze the risk factors implicated in increasing the risk of LOC among 4668 LC cases. They found that chronic obstructive pulmonary disease is a significant independent predictor of LOC with an odds ratio (OR) of 6.03 ($P = 0.03$). Therefore, we can conclude from these studies that although a higher ASA class is not a contraindication for attempting LC, preoperative optimization of this subcategory of patients is crucial.

**Liver Cirrhosis and Portal Hypertension**
Patients with liver cirrhosis are twice more likely to develop gallstones compared to the general population. Furthermore, the morbidity and mortality associated with gallstone disease and its surgical treatment are increased in this subcategory of patients [35]. First, there is a significant increase in the risk of perioperative bleeding secondary to the extensive collateral circulation developed due to portal hypertension and the technical difficulties imposed by the fibrotic liver. Second, and due to the multi-organ dysfunction seen in liver cirrhosis, patients are prone to develop hepatic and renal decompensation under the stress of the surgery and anesthesia itself. Finally, patients with liver cirrhosis have impaired wound healing that increases the risk of postoperative surgical site infection [36] All these aforementioned complications lead the NIH to issue a consensus statement in 1992 that considered liver cirrhosis as an absolute contraindication for LC [37].

However, since then, there has been several publications that showed LC to be a safe surgical alternative in patients with gallstone disease and underlying liver cirrhosis. This is especially true for patients with Child A or B liver cirrhosis [37–40]. In 2003, Puggioni and Wong [38] performed a systematic analysis of articles published between 1993 and 2001 and included 400 cirrhotic patients. This meta-analysis found that LC was superior to OC; it was associated with decreased perioperative blood loss, operative time, and postoperative length of hospital stay with an overall conversion rate of 7%. Machado [40] demonstrated similar results after enrolling 1310 patients through a meta-analysis of articles published between 1994 and 2011. Among these patients, 17 had Child C liver cirrhosis, and these patients had a higher conversion rate (35%) compared to patients with Child A and B liver cirrhosis (4.5%) and increased overall morbidity.

Currently, the existing evidence is not sufficient for definitive conclusions in regard to the laparoscopic approach in cirrhotic patients. Although the conversion rate is higher, LC is neither contraindicated nor associated with a higher morbidity in patients with Child A and B liver cirrhosis. However, and particularly for patients with Child C cirrhosis, OC still has an important role. Nevertheless, the extent of liver disease should be established preoperatively for appropriate patient optimization and counseling. Laboratory workup should include liver function tests and coagulation studies to determine Child's classification and MELD score, as the latter has been shown to be an effective predictor of postoperative morbidity [41].

**Diabetes Mellitus**
Poorly controlled diabetes mellitus (DM) is theoretically associated with autonomic dysfunction and peripheral neuropathy; thus, patients with gallstone disease may not develop symptoms until late in the disease course leading to a delay in the diagnosis, an increased risk of conversion, and overall morbidity following LC [42, 43]. Although cholecystectomy should not be performed electively for asymptomatic gallstone disease [44], the question of whether DM increases the risk of conversion remains controversial as some studies support this postulate [27, 45] while others show no such association [13, 16, 20].

## 9.2.2 Disease-Related Factors

### 9.2.2.1 Acute Cholecystitis and Cholecystitis-Related Complications

AC is characterized by inflammation of the gallbladder secondary to obstruction of the biliary drainage, leading to an increased intraluminal pressure, distension, wall edema, increase in lymphatic and venous pressure, and eventually ischemia, necrosis, and perforation [46]. In 90% of the cases, cholelithiasis is identified, while in the remining 10%, no gallstones are seen and hence, the diagnosis is referred to as "acalculous cholecystitis" [46]. According to the most recent update of the Tokyo guidelines [47], the diagnosis of AC includes (1) local signs of inflammation (local tenderness, pain), (2) systemic signs of inflammation (leukocytosis, fever, elevated inflammatory markers), (3) radiological criteria for cholecystitis (pericholecystic fluid, thickened wall >3 mm, with/without presence of cholelithiasis), and (4) finally a positive murphy sign on physical exam or ultrasound evaluation.

The severity of the underlying inflammatory process in AC is a prime risk factor for LOC and overall morbidity following surgical intervention. This can be predicted preoperatively based on the status of admission (emergency or elective), systemic inflammatory markers, radiological criteria, and clinical presentation [13, 16, 18–20, 25–27, 34, 35]. All these aforementioned variables can predict a “difficult cholecystectomy” that would translate to technical limitations for safe dissection and thus increase the risk of LOC.

For instance, severe inflammatory cases, such as perforation of the gallbladder (seen in 6–18% of AC cases, Fig. 9.1), gangrenous cholecystitis (seen in 2–30% of AC cases) with secondary abscess or empyema formation, and emphysematous cholecystitis (seen in 1% of AC cases) [48–50], result in the formation of dense adhesions around the surgical field and possible encasement of the gallbladder by the omentum. On the other hand, the acutely inflamed gallbladder can

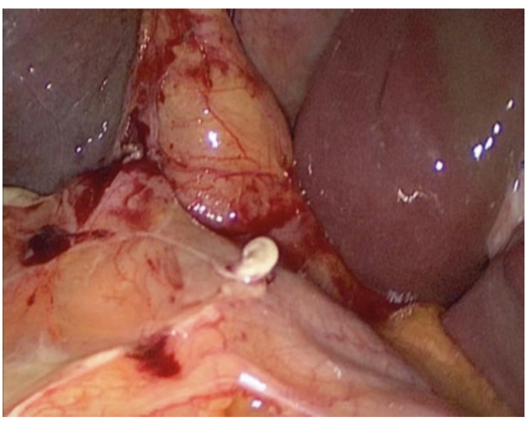

**Fig. 9.1** Severe acute cholecystitis complicated by hydrops of the gallbladder. This patient had several gallstones impacted in the infundibulum and dense omental adhesions secondary to the severe underlying inflammatory process

become shrunken and contracted, shortening the cystic duct and distorting the anatomy of the hepatocystic triangle. Furthermore, the gallbladder might become adherent to adjacent visceral structures such as the common bile duct (CBD), duodenum, and colon. All of these variables combined pose significant technical challenges for the operating surgeon due to an increase in the risk of intraoperative bleeding, iatrogenic injury. That is the reason why, in the face of these challenges, the surgeon might choose to abort the laparoscopic approach and convert to open [48, 50–53]. The presence of any of the three aforementioned complications, based on reports from national registries [54, 55], increases the risk of conversion by threefold compared to uncomplicated AC.

#### 9.2.2.2 Timing of Cholecystectomy

There has been considerable debate on whether the timing of cholecystectomy has any relation to the conversion risk. While some studies showed an increased risk of LOC if LC is delayed beyond 48–96 h of symptoms onset [12, 56], most other retrospective reviews and meta-analyses [26, 57–59] demonstrate that early LC (within 7 days of symptom onset) may be associated with shorter operation time, lower postoperative wound infection rates, and shorter length of hospital. However, delayed LC was not associated with an increase LOC risk. Roulin et al. (2016) [60] performed a prospective randomized controlled study that looked at the timing of cholecystectomy and its relation to clinical outcomes. They randomized 86 patients to either early (within 72 h of symptom onset) or late LC (6 weeks, initial antibiotic therapy). They found that patients with AC operated on within 72 h of symptom onset had lower overall morbidity, shorter median length of hospital stay, and shorter duration of antibiotic therapy. However, there was no difference in the conversion rate between early and delayed LC. Therefore, current evidence advocates early LC (within 72 h) of symptom onset rather than delayed or interval LC due to evidence supporting superior patient outcomes.

#### 9.2.2.3 Mirizzi Syndrome

Mirizzi syndrome develops secondary to a large impacted stone in the infundibulum of the gallbladder that compresses the common hepatic duct leading to obstructive jaundice, cholangitis, and eventually chronic inflammation and fibrosis [61]. It is encountered in 0.3–3% of all LC cases and can be subdivided into two main subtypes [61, 62]. Type 1 is characterized by extrinsic compression of the CBD secondary to a large gallstone in the Hartmann's pouch, while in type 2, the stone erodes through the gallbladder wall into the CBD leading to the development of a cholecysto-coledochal fistula [63]. Preoperative recognition of this diagnosis is crucial, and a high index of suspicion is required to identify this disease entity preoperatively especially in the presence of an empyema, mucocele, or stone impaction. This can be suspected based on cholestatic elevation pattern of liver function tests (LFTs), or on magnetitic resonant cholangiopancreatography (MRCP), or on endoscopic retrograde cholangiopancreatography (ERCP) [64]. Furthermore, a differential diagnosis of gallbladder cancer involving the CBD should always be entertained, as a high association between gallbladder cancer and Mirizzi syndrome was previously demonstrated [65].

Initially, Mirizzi syndrome was considered a contraindication for LC [61], as it was associated with a significant risk of LOC (>50%) and increased morbidity [62]. However, with the advert of alternative laparoscopic approaches such as subtotal cholecystectomy and increased surgeon experience, the laparoscopic approach can be attempted in selected cases, with an acceptable elevated risk of conversion [66].

#### 9.2.2.4 Imaging Parameters

Several findings on preoperative radiological evaluation have been shown to be associated with an increased risk of LOC across multiple prior publications [14, 18–20, 27, 42, 53, 67]. Thickened gallbladder wall, pericholecystic fluid, presence of CBD stone, and dilated CBD- or AC-related complications have all been shown to increase the risk of conversion following LC. In a prospective analytical study conducted by Yadav and Janugade (2019) [18] to determine the predictive factors for difficult LC, they found that a thickened gallbladder wall, impacted stone, and pericholecystic collection are all significant predictors of LOC. Fuks et al. (2012) [67] correlated preoperative CT findings with the risk of conversion prospectively. They demonstrated that the absence of gallbladder wall enhancement (suggestive of gangrenous cholecystitis) and the presence of gallstones in the infundibulum are significant predictors of LOC. Therefore, and based on the aforementioned studies, radiological findings that reflect a severe underlying inflammatory process should be considered as risk factors for an increased risk of LOC.

#### 9.2.2.5 Coledocholithiasis and Gallstone Pancreatitis

CBD stones are detected in 11–25% of all patients with symptomatic cholelithiasis, with the reported incidence reaching 43% in individuals above 80 years of age [23, 68]. For patients with preoperative evidence of coledocholithiasis, clearance of the CBD using ERCP followed by LC is the gold standard treatment modality [69]. However, approximately 10% of patients who undergo LC are found to have CBD stones intraoperatively [68, 70] and with the availability of surgical expertise and the necessary resources, laparoscopic CBD exploration (LCBDE) can be safely performed without an increased risk of LOC [71] Two meta-analyses [72, 73] have demonstrated that patients who undergo LCBDE, as opposed to those who undergo postoperative ERCP as a two-staged approach, have comparable results in terms of overall morbidity and rate of CBD clearance. Therefore, and based on the above, the presence of CBD stone is neither a contraindication for LC, nor does it increase the risk of conversion, if appropriate treatment decision planning is made preoperatively.

Gallstone induced pancreatitis is the most common etiology for acute pancreatitis with varying disease severity [74, 75]. It has been shown that patients with mild–moderate gallstone pancreatitis should undergo early LC, owing to the increased (20–60%) risk of recurrence if the definitive operation is not performed at the initial admission [76, 77]. Furthermore, performing the cholecystectomy in these patients is neither associated with increased complication rate nor an increased risk of LOC [27, 76]. However, in the subcategory of patients with severe gallstone pancreatitis, there is consensus that LC be deferred (preferably 6 weeks after the index episode) until complete resolution of local and systemic inflammation is achieved [76, 77].

#### 9.2.2.6 Chronic Cholecystitis

The chronicity of gallbladder inflammation, most commonly secondary to recurrent biliary colic's, has been shown to be associated with increased technical limitations during an otherwise straightforward LC, and thus may increase the risk of LOC (Fig. 9.2) [78–80]. It is believed that the fibrotic and desmoplastic reaction that results secondary to the chronic inflammatory process distorts normal tissue plane, rendering dissection around the hepatocystic triangle more difficult and surrounding visceral structures such as the CBD or duodenum more prone to iatrogenic injury [80, 81] This is thought to be the primary underlying factor for the increased risk of LOC witnessed in males and in the elderly population [16, 21–24]. Therefore, identifying patients with chronic cholecystitis preoperatively is crucial for surgeon preparation for intraoperative hurdles that will be encountered in chronic inflammatory cases.

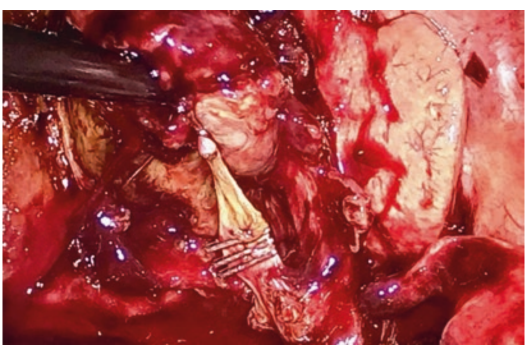

**Fig. 9.2** Severe chronic cholecystitis causing dense adhesions and inflammatory fusion of the triangle of Calot

### 9.2.3 Surgeon-Related Factors

#### 9.2.3.1 Minimally Invasive Surgical Training (MIST)

It has been well documented that the conversion rate from laparoscopic to open cholecystectomy is lower among well-experienced high-volume surgeons and minimally invasive surgical training propitiates this effect [15, 19, 81–84]. Nevertheless, the threshold of conversion varies between surgeons and is related to several subjective variables such as perceived intraoperative difficulty, expertise, and prior training in MIST [14].

In a single-center retrospective study that included 2810 LC cases, Coffin et al. (2017) [15] identified MIST as a significant predictor of conversion on univariate but not multivariate analysis. However, despite the presence of several known risk factors for conversion among the MIST surgeon group, the LOC rate remained significantly lower, indicating that expertise and MIST are independent predictors of conversion. Furthermore, it has been proposed that surgical experience standardizes the basic steps of LC, regardless of the underlying disease severity [83]. Therefore, a well-rounded, structured, educational MIST for surgical trainees can guarantee high patient safety profiles, decrease the conversion rate, and ultimately improve patient outcomes [84].

## 9.3 Risk Scores System and Prediction Models

Numerous studies have attempted to develop a validated risk score for predicting LOC based on several preoperative clinical, radiological, and laboratory parameters [14, 25, 29, 42, 85–87]. However, these risk scores have not been well implemented in clinical practice, owing to the retrospective nature of most of these studies, lack of prospective validation, and lastly heterogeneity in patient selection and surgeon experience [16, 88]. Moreover, with the current advert of variety of strategies and techniques for dealing with a "Difficult cholecystectomy," conversion to open surgery in the face of these challenges has become much less frequently encountered [88]. Beksac et al. (2016) [85] retrospectively reviewed 1335 LC cases to develop a predictive statistical model based on identified risk factors for conversion. Based on four parameters (age, gender, history of abdominal surgery, and alkaline phosphatase level), their model predicted conversion with a sensitivity of 70% and a specificity of 79%. However, given its retrospective nature and patient heterogeneity, implantation remains restricted.

Siddiqui et al. (2017) [87] attempted to develop a risk score based on seven ultrasound findings through a single-center retrospective review of 300 LC cases. They found that a score of >5 has a sensitivity of 80.7% and specificity of 91.7% in predicting a difficult LC and significantly increase the risk of LOC. However, they excluded patients who underwent emergent LC and patients who underwent conversion based in the presence of other comorbidities. As we have shown previously, both of these variables are known risk factors for LOC, thus disregarding them excludes a significant proportion of patients who underwent conversion, putting the generalizability of these results into question.

Lastly, Sutcliffe et al. (2016) [14] developed a validated risk score for LOC based on a prospectively maintained cholecystectomy database from the United Kingdom that included 8820 patients across 166 hospitals. The risk score (CLOC score) was derived from six significant predictors of conversion: ASA class, age, gender, indication for LC, thickness of gallbladder wall, and CBD diameter. They concluded that a score of more than six identified patients at a high risk of conversion (7.1%, with an area under the curve = 0.766 ($P < 0.001$), and therefore, should be operated on by experienced surgeons. However, this study failed to identify the precise indication for conversion. Moreover, they failed to account for several variables that have been shown to exacerbate the risk of LOC including patient comorbidities, prior surgical history, and even the utilization of the critical view of safety during LC. This again puts the generalizability of this risk score to the general population into question.

In summary, the studies that have aimed to develop a statistical model for prediction of conversion are limited by a small sample size, patient heterogeneity, retrospective nature, and failure to account for the "surgeon" variable. Therefore, the applicability of these models and their implementation into clinical practice is limited by the lack of validation and prospective evidence. Nevertheless, although these models can aid in operative planning, recognizing the aforementioned risk factors as significant predictors of conversion and making the necessary treatment decision are key factors in optimizing patient outcomes.

## 9.4 Conclusions

Conversion from laparoscopic to open cholecystectomy is multifactorial in origin and, as we have shown, is influenced by several patient-related, disease-related, and surgeon-related factors. In the setting of an intraoperative complications such as bleeding, or as a means to avoid iatrogenic injury and even if progress cannot be accomplished laparoscopically, the operating surgeon might consider abandoning the laparoscopic approach and converting to open [16, 29]. Several prior reports have shown that patients who do undergo conversion may have an increased length of hospital stay, surgical site infection rates, and possibly overall morbidity [12, 13, 16, 30]. However, conversion should still be considered as one of several alternative options to deal with the "difficult gallbladder." This modality, in the face of intraoperative challenges, should never be considered as a complication nor as a failure on part of the surgeon. Rather, it is a safe option to avoid complications and optimize patient outcomes. Preoperative identification of the cited risk factors for LOC is crucial for appropriate operative planning, surgeon preparation, and, most importantly, improved patient outcomes.

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# 10 Difficult Laparoscopic Cholecystectomy: When to Convert to Open Technique

Fabrizio D'Acapito, Giuliano La Barba, Chiara Togni, and Giorgio Ercolani

## 10.1 Introduction

Laparoscopic cholecystectomy (LC) is the "gold standard" in the treatment of symptomatic gallbladder's lithiasis and is the most performed laparoscopic abdominal surgery in the world.

It is associated with a morbidity rate of around 10% with an increased risk of bile duct injury (0.1–1.5%) when compared to open surgery [1, 2].

In elective procedures, the laparoscopic conversion rate in the open cholecystectomy is low with a range in the literature between 2% and 15% [3–6], while it increases up to 25% when the patient is operated on for acute cholecystitis [7, 8].

There are conditions in which it is not possible to complete the cholecystectomy safely and in such cases deviations from the standard surgical procedure are mandatory.

In the literature, this condition is generically identified as "difficult gallbladder" and represents a challenge for the laparoscopic surgeon.

"Difficult gallbladder" (DGB) corresponds to a procedure with an increased surgical risk compared to standard cholecystectomies and has been reported with an incidence up to 26% in large series [9, 10].

The concept of "difficult gallbladder" is mainly based on intraoperative findings and strongly depends on the surgeon's skills. The pattern of "difficult gallbladder" is characterized by severe inflammation which makes dissection difficult, alters the anatomy, and increases the risk of bleeding [11, 12]. In 2016, among 2212 patients undergoing laparoscopic cholecystectomy in 10 years, Ashfaq A. et al. reported in 351 (15.8%) criteria of difficult gallbladder and among these the conversion rate was 19.9% [11].

In case of acute cholecystitis, chronic or scleroatrophic cholecystitis and cirrhotic liver are more frequently faced with a difficult gallbladder scenario (Fig. 10.1).

Acute cholecystitis is one of the main causes of acute abdominal hospitalization in the adult population and the most common indication for abdominal surgery in the elderly patient [13, 14]. Early laparoscopic cholecystectomy results in a shorter postoperative hospitalization period and lower healthcare costs [7, 15]. In a recent study by Kais H. et al., in 1658 laparoscopic cholecystectomies, the conversion rate increases more than tenfold depending on whether the surgery was

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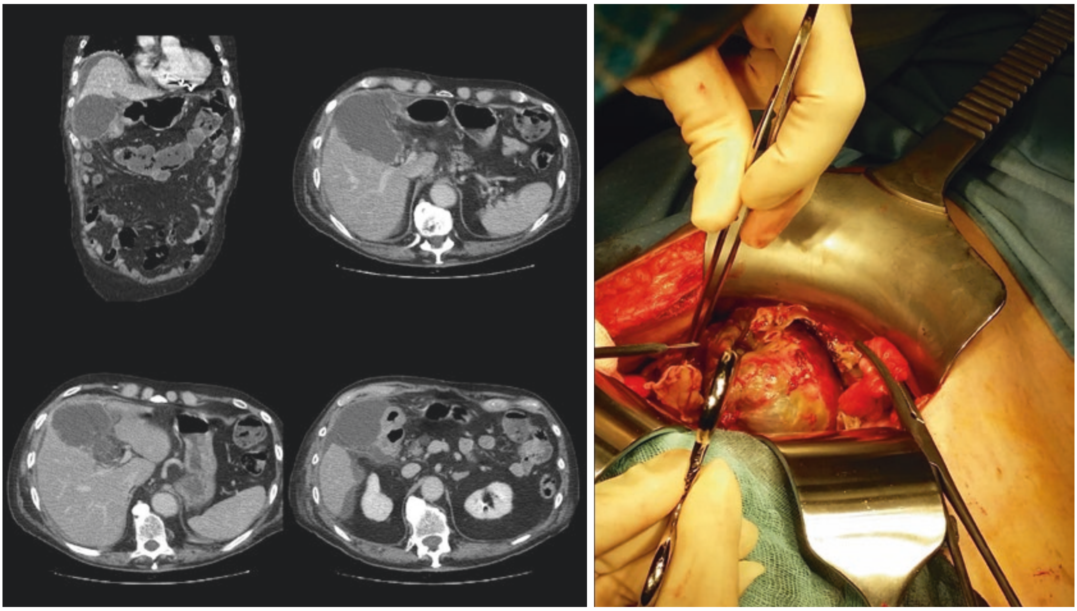

**Fig. 10.1** Sample case: 89-year-old male. Admission to E.R. for abdominal pain for over 48 h. Abdominal U.S: acute acalculous cholecystitis with thickening of the walls and pericholecystic fluid. Medical therapy started. After 24 h worsening of clinical symptoms. CT scan: acute gangrenous cholecystitis, hydrops, peri-cholecystic abscess and perihepatic fluid , with irregularity of the gallbladder wall and the partial lack of contrast enhancement (perforation at the fundus level). Indication for emergency surgery. Laparoscopic approach but early conversion. Right subcostal laparotomy. Intraoperative evidence of: free corpuscular fluid in the abdomen; viscero-parietal and liver-diaphragmatic adhesion; abscess between cholecysts and «falciform ligament» and in the Morrison's pouch. The gallbladder is hydropic, with necrotic areas at the body and fundus level with at least two perforations. An anterograde cholecystectomy was performed leaving a small portion of gallbladder in the cholecystic bed

performed in election or for acute cholecystitis from 2.1% to 24.8%, respectively [16]. In order to univocally define the acute cholecystitis patterns, several scores have been proposed, the most widespread of which are the Tokyo Guidelines in their last revision dated 2018 (TG18). The TG 18 also suggest a treatment flowchart [17–20].

A recent Swedish study reported a doubled risk of bile duct injury (BDI) in acute cholecystitis and showed a statistically significant association between the severity of cholecystitis according to TG18 and BDI risk [21].

Chronic or scleroatrophic cholecystitis can lead to a difficult gallbladder pattern. The Swiss Society of Laparoscopic and Thoracoscopic Surgery analyzed a database of 22,953 patients and found a conversion rate for acute cholecystitis of 15.9% versus 6.4% for chronic cholecystitis. Both are significantly higher than for standard cholecystectomy [3].

Prevalence of gallstones in patients with cirrhosis is estimated at 29–46% and is three times higher than that in patients without cirrhosis [22]. Laparoscopic cholecystectomy in cirrhosis is associated with a morbidity rate between 5% and 23% and a mortality rate between 7% and 20%.

In a review on cholecystectomy in cirrhotic patients, Laurence J.M et al. reported that mortality rates in LC was 0.74% while in open cholecystectomy it was 2%, the conversion rate was 5.8% while the overall complication rate was 17.6% in LC and 47.7% in open [23]. In another review, Machado N.O. documented a conversion rate of 4.58%, 17% morbidity, and 0.45% mortality [24].

Cholecystectomy is more hazardous in cirrhosis because of hemorrhage related to portal hypertension, coagulopathy, and thrombocytopenia [23].

Surgeons around the world, after an initial period in which the majority of them were convinced that the cholecystectomy had to be completed in laparoscopy, soon realized that the procedure had to be converted to avoid complications [25].

A large-scale multinational survey involving more than 500 participants from Japan, Korea, and Taiwan achieved that the commonly used indicators of surgical difficulty during LC, such as the duration of surgery, estimated blood loss, and open conversion rate, are inappropriate as they are surgeon- and workplace-dependent. Safety measures and recognition of landmarks and gallbladder anatomy during LC are performed at the surgeons' discretion and are not yet standardized [26].

Laparoscopic surgeons have been found to have conversion rates to open surgery of one-fourth compared to others [27]. Laparoscopic surgeons tend to persist in laparoscopy even in case of significant lengthening of operating time caused by extensive viscerolysis, Calot fibrosis, or diffuse scarring of the gallbladder bed.

Another aspect to be considered is the training of young surgeons who have less experience in open cholecystectomy. Approximately 20% of surgeons find that conversion to open surgery does not make the procedure safer but sometimes more difficult [26].

In case of a difficult cholecystectomy, it is necessary to make sure to be as much as possible in the condition in which the conversion is an "elective" choice of the operator before being forced to do it as a result of major intraoperative complications.

## 10.2 Risk Factors to Open Conversion

Three types of factor have been identified in the literature that predispose to the conversion of the procedure and are classified as: patient-related, disease-related, and surgeon-related.

The "patient-related" factors are: age over 65 [28], male gender, BMI over 30, history of upper abdominal surgery, ASA score, cirrhosis [24, 29], diabetes mellitus (which can cause a delayed perception of symptoms) [30].

The "disease-related" factors are: gallbladder wall thicknesses (suggesting that a gallbladder wall thicker than 4–5 mm on preoperative ultrasound is a risk factor for conversion.); acute cholecystitis [29, 31], recurrent biliary colic, acute biliary pancreatitis; Mirizzi syndrome (found in 0.3–3%); GB cancer (which should be kept in mind in over 65-year-old patients, female gender, and high level of alkaline phosphatase); lithiasis of the main bile duct [6]; and the following laboratory data: CRP [32], WBC, albumin, and liver function tests [31].

"Surgeon-related" factors are the experience and skills of the surgeon [3, 33–35]. Using these factors, scores and models have been built to predict the conversion risk [6, 31, 36–38].

The pattern observed from these risk scores and models is that the risk of conversion increased when more risk factors were presented.

Defining risk factors for conversion and complications is important when planning the procedure and deciding who should perform the cholecystectomy [39].

In 2018, using the Delphi consensus methodology, Iwashita Y. identified 25 aspects of intraoperative difficulty associated to conversion; among these, diffuse scaring in the Calot's triangle area had the strongest impact on surgical difficulty. Surgeons agreed that the surgical difficulty increases as more fibrotic change and scarring develop [18].

A "universally recognized" codification of the steps of laparoscopic cholecystectomy is essential, in particular, in the difficult gallbladder to limit the risks of BDI and biliary-vascular injury (BVI) [17]. The training of young surgeons should aim at this result.

The primary target of laparoscopic cholecystectomy is "safety first, total cholecystectomy second," and the surgeon should always keep in mind this culture of safety and remain vigilant to stay ahead of dangerous situations. Safe management of the difficult gallbladder is possible with technical adjustment and careful use of bailout procedures.

## 10.3 Safe Steps in Laparoscopic Cholecystectomy in Difficult Gallbladder Pattern and When to Evaluate the Use of Bailout Procedures

We will develop the discussion by proposing a procedural algorithm built on the "Safe Step in Laparoscopic Cholecystectomy for Acute Cholecystitis" identified by Wakabayashi in the TG 2018, inserting moments of "time-out" in which the most common difficulties that can be found in the different steps will be identified, and codified solutions will be proposed (Fig. 10.2). In the next section of the chapter, we will examine in detail the bailout techniques.

The first assessment of the procedure should be made before carrying the patient to the operating room. It is necessary to assess with the anesthesiologist, depending on the anamnesis (COPD, cardiovascular diseases, previous surgery, especially of the upper abdomen, etc.) and the patient's condition at the time of surgery (grade of cholecystitis according to TG18), whether he is able to tolerate pneumoperitoneum for an adequate operative time, also evaluating in advance the possibility of a long and complex viscerolysis [12].

If the patient's condition is very damaged, consider the possibility of using percutaneous cholecystostomy as a definitive management or "bridge" to surgery [40].

## 10.4 In Operating Room

### 10.4.1 Step 1

A specific patient position is not considered as being better (French Vs American) [19].

In patients who have already been operated on, the site of the first port must be carefully chosen [41], also in variance with what is considered, the standard setting used in the surgical unit, in order to reduce the risk of being in an adhesion tangle that could lead to visceral iatrogenic lesions from the time of peritoneal access [12]. The method of placement of the first trocar should be tailored to the patient's characteristics. The open trocar insertion is a safe technique [42]. In cirrhotic patients, the first port was placed, with the open technique, in the midline sub-umbelically to avoid undetected enlarged collateral vessels [43].

Once the pneumoperitoneum has been established, it is necessary to evaluate the extent and characteristics of the adhesions to assess the complexity and risk of iatrogenic lesions from viscerolysis and the possibility of a significant increase in surgical time compared to an open procedure [44]. This is a good time to decide on an early conversion.

In a patient where the supramesocolic district is inaccessible due to adhesions, perhaps between the transverse colon and the parietal peritoneum, a right subcostal laparotomy could allow access to the cholecystic lodge avoiding prolonged and risky viscerolysis maneuvers. The same applies if there are adhesions that significantly hinder the setting of two or more trocar. Usually the lysis of adhesions caused by an acute cholecystitis is all the easier the earlier the intervention is performed compared to the onset, while the exacerbation on previous acute episodes usually leads to tenacious adhesions. During viscerolysis maneuvers, it is advisable to proceed as far as possible to dissect using cold scissors [41]. In case of the first episode of cholecystitis, especially if the intervention is performed early at the onset of symptoms, the adhesions are smoothed out. In case of relapse on chronic cholecystitis or in case of covered perforation, the adhesions can be tenacious. Viscerolysis should be performed particularly carefully to avoid injury to the duodenum, which may be attached to the gallbladder (Fig. 10.3).

### 10.4.2 Step 2

Once the gallbladder has been visualized, the possibility of its mobilization must be evaluated.

The mobilization of the gallbladder is a key point because it allows the correct exposure of the hepatocystic triangle. A correct mobilization involves a traction with fundus clamp towards

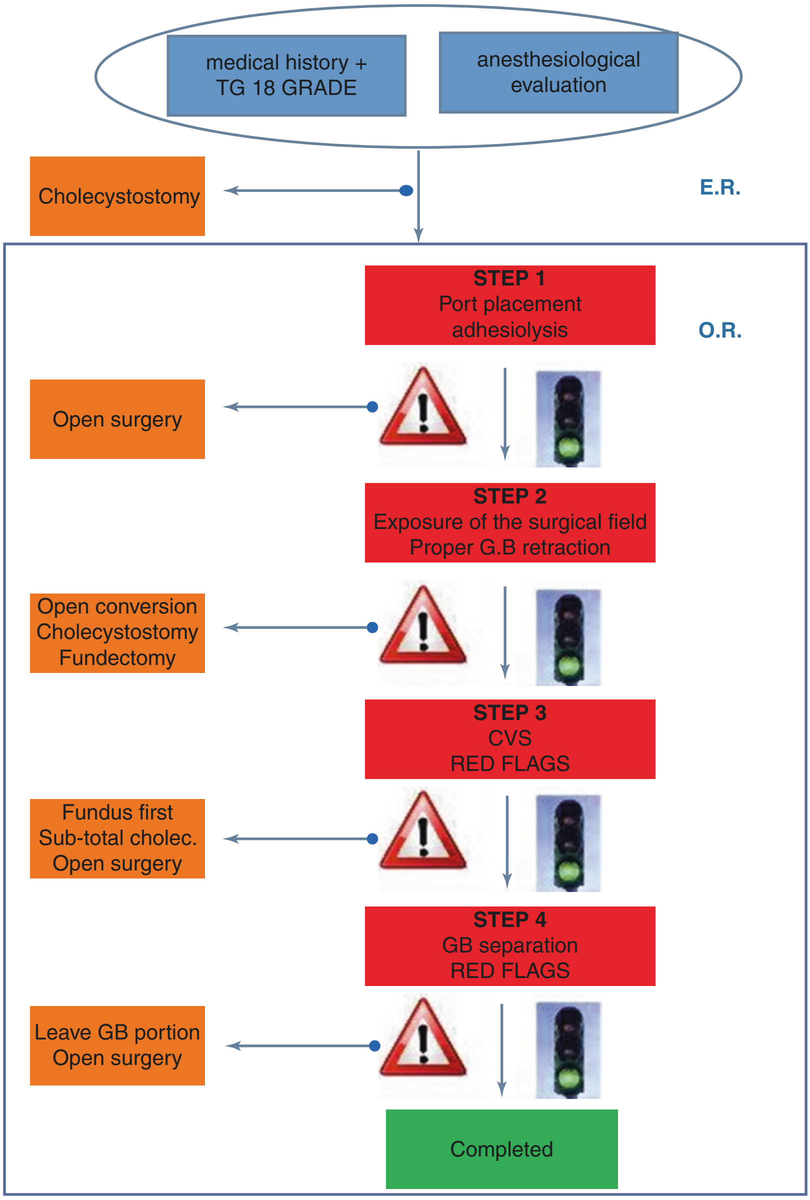


**Fig. 10.2** Safe step in laparoscopic cholecistectomy: If the individual steps cannot be completed safely, Bail-out methods are suggested

the right shoulder of the patient associated with a traction with a second clamp positioned on the Hartmann pouch downwards and to the right [45]. Surgeons should keep in mind that decreasing the number of port and/or using smaller instruments may create technical challenges, due to more difficult retraction and triangulation [19]. In the case of an outstretched gallbladder (hydropic or emphysematous), prior needle aspiration results in decompression with minimal intraperitoneal contamination [46] (Fig. 10.4). Once aspirated, it is necessary to evaluate the thickness and consistency of the walls of the gallbladder. The use of an endograsper or the placement of one or more traction points on the bottom can mobilize the most demanding gallbladder. Usually the bleeding resulting from the trauma of the gallbladder wall is annoying but not significant.

The presence of large necrotic areas can preclude the possibility of performing a valid

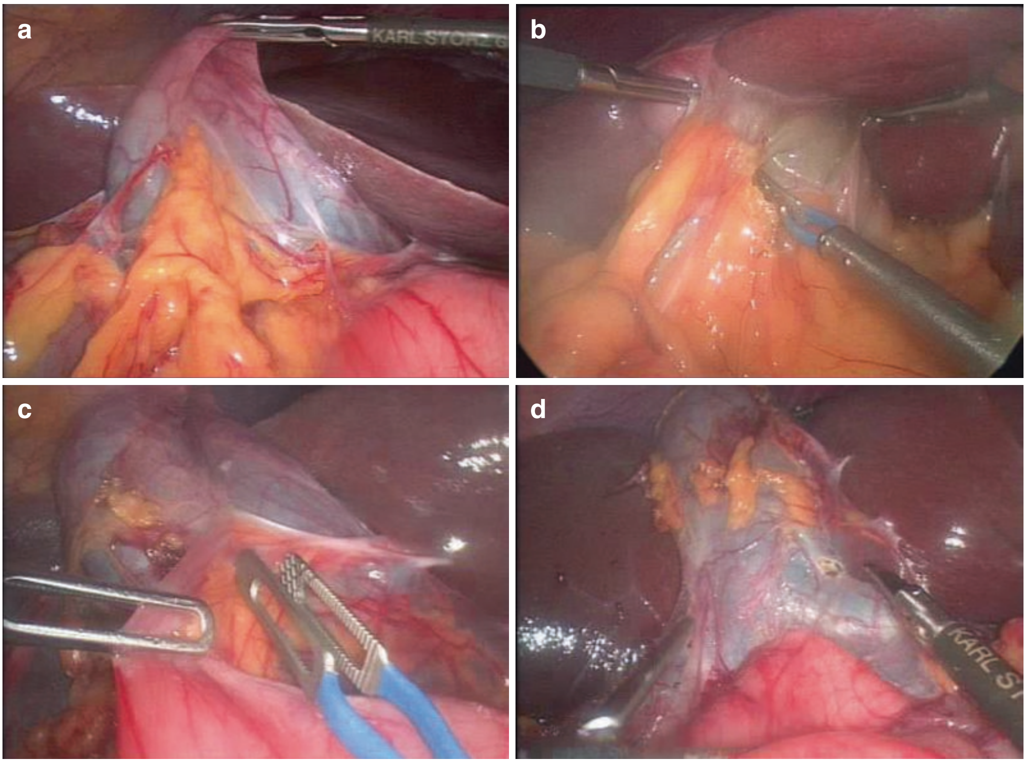

**Fig. 10.3** Examples of different types of adhesions: (**a**) cholecysto-omental adhesions; (**b**) cholecysto-omental adhesions with acute cholecystitis edema; (**c**) bridge of adipose tissue binding the stomach to the gallbladder; (**d**) the first duodenal portion is fused to the gallbladder

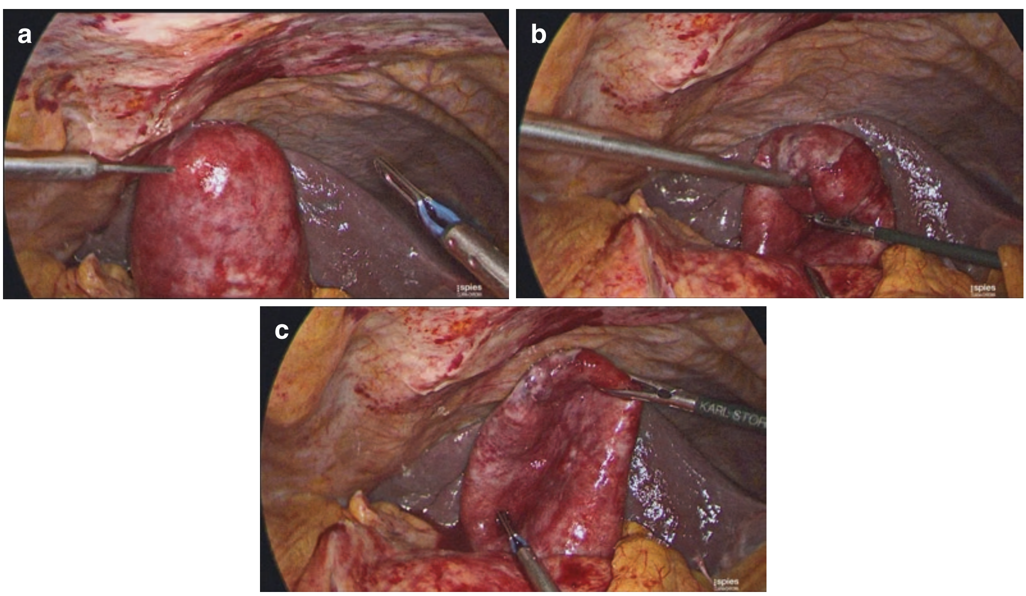

**Fig. 10.4** Outstreatched gallbladder. (**a**) A suction needle is introduced from the port on the right side (always under direct vision). (**b**) The emptying of the gallbladder can be facilitated by cautious compression (milking) maneuvers performed with a clamp. (**c**) At the end of the procedure the prick area is grasped with the forceps in order to limit as much as possible the outflow of residual bile

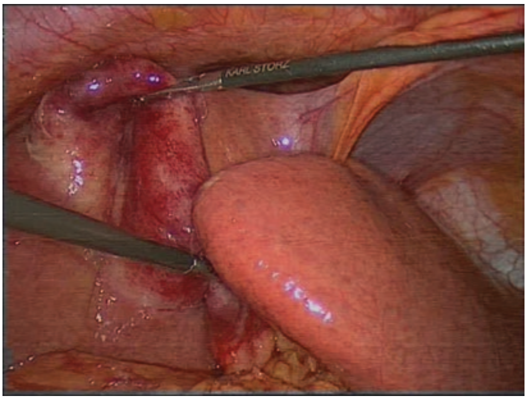

**Fig. 10.5** Steatosic liver with segment 3 hypertrophy hiding the hepatocystic triangle

gallbladder traction, while the presence of perforations with constant outflow of pus, bile, and calculi can make the evaluation of the operating field very complex.

Even a bulky calculus impacted in the infundibulum can limit the possibility of mobilization of the gallbladder; often cautious maneuvers with the aspirator or with forceps allow the infundibular calculus to dislodge towards the gallbladder body [47].

Another element to take into account is the liver. The presence of segment 3 or 4 hypertrophy covering the hepatic pedicle may require the use of a retractor to visualize the cholecystic hilum or may force the use of incorrect traction to visualize the hepatocystic triangle (Fig. 10.5).

Liver texture is another important variable because tractions on a steatosic liver can lead to lacerations with subsequent bleeding while a cirrhotic liver can be very difficult to mobilize because it is hard and fibrotic [43]. The adhesions in the cirrhotic patient may be hypervascularized. Furthermore, the finding of signs of portal hypertension should lead to a careful reconsideration of the therapeutic strategy chosen for the high risk of bleeding [43].

### 10.4.3 Step 3

#### 10.4.3.1 Critical View of Safety (CVS)

The CVS is not a dissection technique. It is the final view that is achieved after a thorough dissection of the hepatocystic triangle to delineate the cystic duct and the cystic artery before they are clipped and divided. The CVS should be seen clearly both from the front and the back to have a complete circumferential visualization of the cystic duct and the artery (doublet view). The anterior view is easily achievable by retracting the infundibulum inferolaterally towards the right (with segment 5 surface visible across window), while the posterior view requires the infundibulum to be retracted towards the umbilical fissure (with segment 4/quadrate lobe surface visible across window). Dissection has to lead to the creation of 2 windows, one between the cystic duct and the artery and one between the artery and the liver. The cystic plate must be clearly identified [48].

To obtain the CVS, the coded technique involves three steps [49]:

(a) Clearance of the hepatocystic (HC) triangle: The HC triangle should be cleared of all the fibrofatty and soft areolar tissue. Once adequately cleared of all fibrofatty tissue, the under surface of the liver is easily seen across this triangle.
(b) Exposure of the lower cystic plate: The gallbladder should be separated from its liver bed to expose at least the lower third of the cystic plate.
(c) Two and only two tubular structures should be seen entering the gallbladder: The cystic duct and the cystic artery [19] (Fig. 10.6).

Because of inflammation of the tissues of the hepatocystic triangle, the maneuvers often cause bleeding. For persistent bleeding, the surgeon must achieve hemostasis primarily by compression and by avoiding the excessive use of electrocautery or clipping [18]. The same gallbladder should be used as a compression instrument for parenchyma; the use of gauze and/or local hemostatic (e.g., oxidized cellulose) should also be considered [50]. There is a low level of evidence in favor of recommending a source of energy compared to another regarding safety. Bipolar, monopolar, and ultrasonic devices are appropriate source of energy for safe cholecystectomy [19]. If a monopolar energy device (most of the one with hook cautery) is used, it is important to keep it at a low setting; divide a small amount of

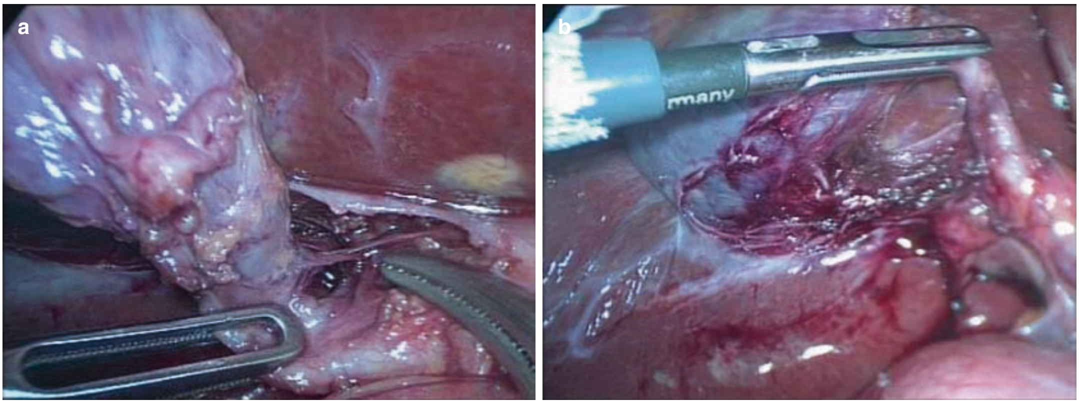


**Fig. 10.6** The CVS should be seen clearly both from front (**a**) and the back (**b**) to have complete circumferential visualization of cystic duct and artery (doublet view). The HC triangle has been cleared of fibroadipose tissue, the gallbladder has been removed from the bottom third of the cystic plate, and 2 and only 2 structures are seen entering the gallbladder

tissue at a time after a gentle pull to avoid injury to deeper structures by the heel of the hook cautery; use intermittent short bursts of current at 2–3 s intervals in order to avoid thermal spread to the bile duct; and avoid blind use of cautery in the case of brisk bleeding [48, 51].

Bipolar cautery is useful to control bleeding in the HC triangle and in the liver bed.

Sometimes, the volumetric increase in Mascagni's lymph node (usually a landmark for cystic artery localization) makes it difficult to identify the cystic artery and gall bladder neck. In addition, in recurring inflammation, Rouviere's sulcus is often erased and not displayed correctly. In these cases, it is desirable to start the dissection very high in contact with the wall of the gallbladder, to which one must always remain attached, and then proceed on both sides to the gallbladder bed [52] (Fig. 10.7).

In chronic cholecystitis, inflammatory adhesions can melt the wall of the gallbladder to the wall of the common liver duct. If a biliary-cholecystic fistula is suspected at this stage, strongly consider a bailout technique [53].

In presence of severe acute and/or chronic inflammation, secure ductal identification by the critical view of safety (CVS) may be very challenging.

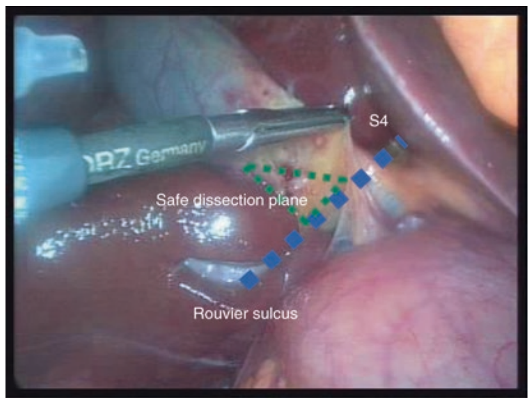


**Fig. 10.7** Rouviere's sulcus. The sulcus indicates reliably the plane of the CBD; dissection may be started safely by division of the peritoneum immediately ventral to the sulcus and continued in a triangle bounded by the plane of the sulcus, the neck of the gallbladder and the liver surface

During "Step 3," it may also be useful to stop several times, widen the view of the surgical field, reevaluate our landmarks, and then resume the isolation maneuvers.

In accordance with the data in the literature, we have identified the warning signs, which we will call "red flags," to which particular attention should be paid during the acquisition of the CVS [47].

#### 10.4.3.2 Red Flags

(a) More than two tubular structures entering GB [48].
(b) An unusually large presumed cystic artery (this may be the hepatic artery). The cystic artery is usually single, originates from RHA, and most commonly traverses the HC triangle. If the presence of a short cystic artery (<1 cm) is not noted during surgery, the right hepatic artery may be clipped and divided [54]. Keeping the dissection of the artery close to the gallbladder on the right side of the cystic lymph node may prevent injury to the right hepatic artery [47]. It may be useful to isolate a longer-than-usual tract of the artery to check whether it has penetrated the hepatic parenchyma or ended up in the gallbladder.
(c) Large artery pulsations behind the presumed cystic ducts (this duct may be common hepatic duct).
(d) A medium-large clip fails to occlude the ductal lumen (this duct may be the common hepatic duct) [55].
(e) Large ductal structure that can be traced behind the duodenum.
(f) Excessive fibrofatty/lymphatic tissue noted around the presumed cystic duct.
(g) Bile leak seen with intact GB: See dedicated paragraph.
(h) Bleeding requiring blood transfusion.

In persisting doubt, ask for a second opinion if available [56].

#### 10.4.3.3 Warning

Alternative techniques to the standard exist and are implemented to obtain access to the cystic duct but they do not respect the principles of CVS.

The most widespread is the infundibular approach [57].

In the infundibular technique, cystic duct identification is based on the appearance of the infundibulum–cystic duct junction as a funnel. When this junction is circumferentially exposed, the surgeon confirms the identification of the cystic duct and then proceeds with its division. Complete dissection in the HC triangle is not performed at this stage. In certain situations, this technique can be misleading. When the cystic duct is fused with CBD due to acute or chronic inflammation, when the cystic duct is very short or effaced by a large stone impacted in the infundibulum, or when there is difficultly in exposing the HC triangle due to inadequate retraction, the CBD may be misidentified as the cystic duct. Circumferential dissection then goes around the CBD rather than around the cystic duct across the HC triangle. This leads to classic BDI where the bile duct is divided twice before the gallbladder can be completely separated from the liver. Therefore, this technique of cystic duct identification does not protect against biliary injury in difficult situations [48, 58–60].

The fundus first approach has been described as an alternative technique to complete LC in the presence of severe inflammation in the HC triangle. The gallbladder is dissected off its liver bed and then the cystic duct and the artery are identified and divided. However, the surgeons must be wary of this technique, they should have clear understanding of the cystic plate anatomy and pathological alteration affecting it, they should remain very close to the gallbladder throughout the dissection, and when such dissection does not seem possible, they should resort to bailout techniques like subtotal cholecystectomy (see dedicated paragraph).

Surgeons using this technique should be aware of this possible mishap [47].

Only after obtaining the CVS, surgeons should proceed to dissecting the artery and cystic duct [61].

### 10.4.4 Step 4

GB separation from its bed leaving behind the cystic plate attached to the liver.

Also, in this phase surgeons should pay attention especially in cirrhotic liver, scleroatrophic cholecystitis, and in partially intrahepatic and necrotic cholecystitis. It is better to leave a small portion of gallbladder in the cholecystic bed rather than enter the hepatic parenchyma in that site [43, 62].

Firstly, there might be troublesome bleeding from liver parenchyma, especially if the terminal tributaries of the middle hepatic vein (which lie in this location) are injured. This type of bleeding may sometimes require a conversion to open surgery for its control [62].

Secondly, sub-vesical bile ducts may be injured, causing a postoperative bile leak [63].

Such a breach is more likely to occur in chronic cholecystitis where the gallbladder may be densely adherent to the underlying liver without distinct dissection planes [64].

### 10.4.5 Special Issue: Bile Leak Seen with Intact GB

If bile appears in the operating field, you must identify the source of the leak. Do not proceed with blind dissections in search of the possible source [65], but try to obtain CVS. Once the cystic duct has been identified, perform an i.o. cholangiography to confirm and define the location and extent of the biliary injury [66, 67]. There is no evidence that IOC could prevent BDI [68–70], but IOC is recommended in order to define unclear anatomy [19]. In extreme cases, a cholangiography by direct puncture of the gallbladder can also be attempted. After the staging of the injury, you should make an evaluation of your experience in biliary surgery and decide how to proceed. In case of limited biliary surgery experience, it is preferable to drain the abdomen, even in laparoscopy, and refer the patient to a dedicated hospital. In case of partial lesion of the common bile duct, an attempt to suture on a tutor may be indicated, but always consider the technical experience of the surgeon and the stage of inflammation. In case of complete sections of CBD or complex lesions, it is advisable to stop the procedure, drain the abdomen, and send the patient to a reference center [67, 71].

If you convert the laparoscopic procedure into open surgery to define the extent of the lesion, you should not proceed with an extensive dissection of the hepatocystic triangle if you are not sure that the problem can be properly solved.

## 10.5 Bailout Procedures

In situation of a difficult gallbladder, when the target (cystic duct, cystic artery, and CBD) identification with the CVS cannot be properly achieved, it is not important to push ahead with the goal of a complete cholecystectomy while risking the patient's safety due to potential biliary/vascular injury. It is important to perform an alternative procedure that allows the surgeon to complete the procedure in a safe manner [47].

Bail-out techniques include: cholecystostomy, partial cholecystectomy and conversion to open surgery. In addition to these one should consider the fundus first approach, which is a hybrid way to try to complete the cholecystectomy laparoscopically, adopting the open surgery approach from the bottom of the gallbladder, with the possibility to conclude in a partial cholecystectomy.

The use of these methods should not be considered as a failure, but on the contrary as an integral and responsible part of the patient's path of care and as a way to safeguard his/her health.

The operating surgeon should not hesitate to seek a second opinion whenever needed, and this should be considered as a sign of good clinical practice rather than a sign of surgical incompetence.

### 10.5.1 Cholecystostomy

Tube cholecystostomy could be a simple bridge procedure to provide symptomatic relief until a definitive procedure can be performed. It can be done percutaneously, laparoscopically, or after conversion to open surgery [40, 72–74].

#### 10.5.1.1 Percutaneous Cholecystostomy

A percutaneous cholecystostomy tube serves an important function for patients with cholecystitis who are unable to undergo immediate cholecystectomy safely. An increasing TG18 Grade and comorbidity status are the primary predictors of need for cholecystostomy [75]. If the patient is a poor candidate for general anesthesia, has had symptoms for more than 72 h, or has an advanced metastatic disease, PTC is considered [73, 74]. A trans hepatic approach is typically chosen to enter the gallbladder, with moderate sedation used for nearly all cases. Tube placement procedures were performed by the interventional radiologist with US or CT guidance.

#### 10.5.1.2 Laparoscopically Cholecystostomy

During a laparoscopic approach, the decision to proceed with cholecystostomy is related to the finding of a gangrenous gallbladder and severe inflammation of the HC triangle in a patient in severe general condition. Laparoscopic cholecystostomy is performed when the intraoperative finding shows a condition in which a cholecystectomy cannot be performed safely [76]. The procedure can be facilitated by the use of the laparoscopic ultrasound guidance. An 18-gauge needle was inserted in subcostal position at the midclavicular line into the gallbladder. Once the bile has been aspirated, a guidewire is placed within the lumen of the gallbladder. Over the guidewire, a 14 F catheter is placed into the lumen of the gallbladder and secured to the skin. If there is a rupture on the gallbladder wall, it is easier to empty the gallbladder with the aspirator and then place a catheter with a balloon inside the gallbladder so that it can be safely fixed (without spillage) to the abdominal wall [77, 78].

#### 10.5.1.3 Open Cholecystostomy

The same procedures performed in laparoscopy are also available in open surgery [47].

In most cases when a surgical cholecystostomy is performed, the preoperative assessment is probably not adequate.

### 10.5.2 Fundus First

In case of diffuse inflammation of Calot's triangle, continued dissection to obtain the CVS might result in BDI [79] and an anterograde approach may represent an alternative to immediate conversion to open cholecystectomy [80–82].

Requirements for a safe dome-down technique are: (a) clear understanding of the anatomy of the cystic and hilar plates [83]; (b) the dissection should be maintained along the subserosal-inner layer to avoid vascular and/or biliary injury [19].

The procedure involves the following steps:

1. The gallbladder is dissected away from the gallbladder bed from the fundus down towards the cystic duct [83].
2. Dissection then continues along the gallbladder [84]. The cystic artery is identified, isolated, ligated, and transected.
3. The cystic duct is positively identified and isolated, creating a 360-degree view of the gallbladder–cystic duct junction.
4. The cystic duct is ligated and divided.

This technique poses a technical challenge in handling the gallbladder, as it tends to twist once separated completely from the liver, and also in liver retracting.

In chronic cholecystitis with a small and contracted gallbladder, the longitudinal length of the cystic plate from the fundus to its attachment with right portal pedicle sheath becomes short. Without appreciating this pathologic shortening, the surgeon may enter into the right portal pedicle sheath soon after dissecting the fundus/body of the gallbladder. This may cause injury to the right portal pedicle structures causing serious VBI [64].

### 10.5.3 SubTotal Cholecystectomy

In 1954, McElmoyle first [85] described and illustrated the principles and technique of this operation when performed specifically for the prevention of bile duct or vascular injury during a difficult cholecystectomy. No attempt is made to dissect the cystic duct or artery when inflammation obscures the neck of the gallbladder. The gallbladder is opened and the redundant portions excised. The cystic duct and the portions of the body, neck, and infundibulum lying above and to the left side are left in situ as a shield to the vulnerable structures, then renamed "Shield of McElmoyle." The cystic duct is not closed; its mucosa is ablated and a drain is placed.

Thirty years later, Bornman and Terblanche [86] described their experience in managing difficult gallbladders in cases of severe cholecystitis. Bickel and Shtamler in 1993 describe their successful experience in the treatment of six patients with the use of laparoscopic subtotal cholecystectomy [87].

In literature, "partial," "subtotal," "insufficient," and "uncompleted" are different terms used to define the same concept. Strasberg in 2016 suggested that the term "subtotal" should be preferred since it expresses the nearly complete removal of the gallbladder.

It is important to remove all stones from the gallbladder, to ablate the mucosa of the gallbladder stump (with diathermy or argon plasma coagulator) and leave this stump as small as possible.

#### 10.5.3.1 Technique [88]

The modern technique to perform these operations is clear and can be performed both laparoscopically and in open surgery. The gallbladder is opened along its long axis and emptied of stones, including those in the lumen of the gallbladder neck and cystic duct if possible. Surgeons are recommended to remove all stones from the peritoneal cavity, if necessary, by placing them in an endo-bag. The portion of the gallbladder adherent to the liver is usually left in situ and ablated. The latter may be done with electrocautery, a bipolar forceps, an argon beam, or saline-linked radiofrequency ablation. Alternatively, some or all of the gallbladder attached to the liver may be removed. When this is done, the gallbladder wall and cystic plate may be removed down to the bare liver or the cystic plate may be left in situ. In some cases, the gallbladder will be gangrenous. If so, the gangrenous portion should be excised without widening the extent of the subtotal resection. In a cirrhotic patient, the risk of bleeding from the liver bed may be theoretically avoided in subtotal cholecystectomy by not removing the posterior GB wall.

The area should be carefully drained. The gallbladder lip is usually somewhat larger and the lumen is closed by sutures [88, 89].

The patient must be informed that a gallbladder remnant may result in the formation of new stones with the risk of a new cholecystitis with a possibly challenging preoperative cholecystectomy [90].

#### 10.5.3.2 Cross-Check the Different Techniques

Based on the meta-analysis of Elshaer and coworkers, on a sample of 1231 subtotal cholecystectomies, in 72.9% of cases the procedure was performed laparoscopically. They found low rate of postoperative BDI (0.08%) but higher rates of bile leak (18%), particularly in open procedures. These fistulas seem to resolve spontaneously in most cases within 2 weeks [89].

More patients whose surgery ended with a drainage left under the cholecystic bed because the stump of the neck of the gallbladder was not closed underwent postoperative ERCP compared to those in whom closure was successfully performed, but there was no change in the rate of complications [91].

Based on the meta-analysis of Elshaer and coworkers, it seems that a subtotal fenestrating cholecystectomy is more likely to be done when an open approach is used [89].

Paradoxically, in their data, bile leaks were more common after a laparoscopic procedure. Possibly, this is due to the improved ability to suture the cystic duct orifice when the procedure is done in open surgery [89].

Based on presently available information, it would seem that the fenestrating type of subtotal cholecystectomy would be preferable, but knowledge in this area is very incomplete.

There is no enough information regarding the incidence of symptomatic gallbladder remnants after subtotal cholecystectomies [91].

Laparoscopic subtotal cholecystectomies generally produced better outcomes compared with open subtotal cholecystectomies, but nonsignificant differences were found between the technique of closure or nonclosure of the cystic duct or gallbladder stump and removal compared to the nonremoval of the gallbladder posterior wall [89].

### 10.5.4 Open Conversion

In the past, difficult cholecystectomy was strongly associated with conversion to open surgery. More recently due to decreasing experience in open surgery, alternative tricks are considered before resorting to conversion [19, 92].

The need for conversion is often related to a problem of gallbladder mobilization or the need to control a massive bleeding.

It is important to realize that simply converting to an open procedure does not safeguard against bile duct/vascular injury [93]. A difficult procedure may remain difficult even after conversion to open surgery with no effect on postoperative complications [94].

When setting up the operating room for acute cholecystitis or when we suspect a difficult gallbladder, it is a good rule to prepare the operating bed for the placement of poles to anchor the retractor for the right hypochondrium.

When converting the procedure into open surgery, you need to have a few landmarks in mind.

(a) The abdomen should be deflated before incision, as the pneumoperitoneum distorts the abdominal wall anatomy. Subcostal laparotomy is made 2 to 3 fingerbreadths below the ribs (Fig. 10.8). The incision should allow ideal access to the hepatic pedicle; if necessary, it is preferable to extend it to the left [62].

(b) When the cause of conversion is the difficulty in identifying or releasing the gallbladder, the first point to find is the anterior margin of the liver. It is necessary to begin the release possibly starting from the right side of the gallbladder and then moving to the left. When the bottom of the gallbladder is discovered, if possible, it is grasped with a ring clamp and the release continues on the lower face of the gallbladder, descending towards the Winslow which the surgeon should explore using his index finger. The round ligament then is divided (except in cirrhotic patients), and a retractor is placed. In the most difficult cases, where adhesions due to inflammation or previous surgery have made the structures unrecognizable, more effort is required; the hepatic flexure of the colon and duodenum may be mobilized to the left.

Placement of sponges behind the liver to lift it forward is often helpful with exposure.

Use the Bismuth maneuver of straightening the hepatic peduncle for the correct identification of CBD: downward traction of the duodenum with a sponge and upward traction of the S4 base [52].

(c) When the rearrangement of the hepatic pedicle makes the management of the cystic pedicle dangerous, it is advisable to continue by anterograde approach [95].

Depending on the adherent inflammation pattern, the detachment of the gallbladder from its bed can be started at the intermediate portion.

In chronic cholecystitis with a small and contracted gallbladder, the longitudinal length of the cystic plate from the fundus to its attachment with the right portal pedicle sheath becomes short. This may cause injury to the right portal pedicle structures causing serious BDI/VBI when the surgeon enters into the right portal pedicle sheath.

Despite the dome-down approach, if it is not possible to safely isolate and manage the cystic duct and cystic artery, consider performing a subtotal cholecystectomy.

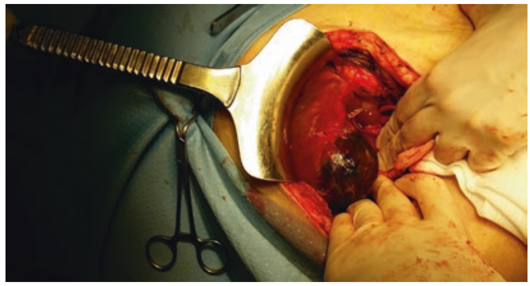

**Fig. 10.8** Conversion to open surgery for acute gangrenous cholecystitis. Large right subcostal laparotomy allowing optimal control over the H-C triangle

(d) Recurrent episodes of cholecystitis can lead to the formation of biliodigestive fistulas (with the duodenum or colon). Cholecystic duodenal fistulas are the most common [96]. The finding is in most cases occasional, and the presence of a fistula must be suspected when you are locked on a very tight adhesion. We proceed by isolating the fistula on both sides. The detachment between the two organs will occur on the cholecystic side. Usually, the fistula is small, and once the healthy margins of the duodenum are prepared, a suture can be performed.

Less often the situation can be more complex: the duodenum is fused between a scleroatrophic gallbladder and the CBD. It is advisable to empty the gallbladder and try a cholangiographic study before deciding what strategy to take.

Cholecystocolic fistulae usually affect the bottom of the gallbladder. Their isolation is easier. They can be treated with either a mechanical suture or a direct suture on the colic side [97].

Fistulas between gallbladder and bile duct deserve separate treatment and will not be the subject of this work.

(e) In case of bleeding from the HC triangle not controlled by compression, consider using the Pringle maneuver as an alternative to achieve temporary hemostasis and identify the source of bleeding. Sometimes it is enough to compress the pedicle between the fingers. Avoid placing stitches blindly or extensive blind coagulation.

In case of bleeding from the gallbladder bed, try compression with gauze and contact hemostatic. As far as possible try to identify whether the source of bleeding is from the roots of the suprahepatic vein [50].

## 10.6 Conclusions

Laparoscopic cholecystectomy is the gold standard for the treatment of gallbladder symptomatic lithiasis. To decrease the incidence of BDI during LC, an effective surgical education system is imperative [98]. While it is easy to underestimate LC as a basic general surgical procedure, the operation may actually be one of the most difficult challenges unexpectedly facing the general surgeon, who should adopt a mindset of "preparing for the worst." In nearly 20% of cases, there is a difficult gallbladder situation that makes the procedure a challenge for the surgeon.

We should always keep in mind that the procedure is performed for a benign pathology. Routine adoption of Culture of Safety in Cholecystectomy (COSIC) may help reduce the incidence of post cholecystectomy biliary/vascular injury [47].

While strict adherence to the CVS is important to decrease BDI, it is only one part of the COSIC, which mandates safety to be at the forefront. Besides achieving the CVS in cases of total cholecystectomy, COSIC also requires an appropriate selection and workup of the patient, the adjustment of the surgical technique in the setting of nonroutine cases, the use of bailout procedures, and the avoidance of complex cases when appropriate experience is not available [99].

A key concept when performing a difficult cholecystectomy is to promptly recognize that change in surgical strategy may result in minor risk of bile duct injury. The conversion of a laparoscopic cholecystectomy to an open procedure should not be experienced as a failure.

Despite overall low incidence of adverse events during LC, the high rate of LC leads to a significant absolute number of patients who suffer from long-term adverse events, one of the most significant being BDI. Otto Von Bismarck once said "Fools say they learn from experience; I prefer to learn from the experience of others."

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# 11 When Is It Safe to Continue Laparoscopically?

Cecilia Chambon, Pablo Valsangiacomo, and Luis Ruso Martinez

## Abbreviations

| | |
|---|---|
| BDI | Bile duct injury |
| CBD | Common bile duct |
| CVS | Critical view of safety |
| IOC | Intraoperative Cholangiography |
| HPB | Hepato-pancreatic-biliary |

## 11.1 Introduction

Laparoscopic cholecystectomy is one of the most frequently performed surgical procedures in the world, with epidemiological differences and areas with different prevalence. This requires health systems to rationalize expenses, including excellence in quality of results and avoid legal medical litigation to surgeons.

The main purpose of biliary surgery safety is the removal of the gallbladder without bile duct injury (BDI) or the vascular structures of the liver pedicle, with a minimum invasion.

Laparoscopic surgery has solved this with an acceptable conversion rate, up to 15% [1].

The safety of a surgical procedure is determined by the ability to perform surgery without increasing the surgical risks and to resolve complications that may occur during the procedure.

Advances in the prevention of bile duct injuries can be summarized in: the development of the concept of "difficult cholecystectomy" and the derivations of it, the critical view of safety of Strasberg [2], conversion indicators, and technical alternatives to cholecystectomy. All these have been useful to the development of the concept of safe cholecystectomy and the idea of a culture of safety for this procedure.

The term "difficult cholecystectomy" is an extensive, complex, and difficult to define concept in the intraoperative time. It can be said that it is a set of pathological situations that technically prevent cholecystectomy in a regular manner. It refers to cholecystectomy under certain situations that do not allow safe dissection, leading to an extension of surgical time and the risk of complications. In a practical sense, we can say that "risk" is implicitly associated with "safety deficit" during a procedure that both factors have a proportional connection and that the resulting decision has an impact on the outcome of the surgery. There are well-established concepts, vast experience, and literature regarding preoperative risk factors for vascular and/or biliary surgical injury, as well as the intraoperative factors that determine the decision to convert or change tactic to more limited surgeries. Under these circumstances, it is considered that the incidence of complications of the main bile duct as well as vascular structures are 2 to 5 times

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higher in laparoscopic cholecystectomy than in the open one [3].

The objective of this chapter is to analyze intraoperative indicators and the logistical context essential to safely continue with a laparoscopic cholecystectomy, mainly technical, linked to dissection and its difficulties. We will not analyze other factors such as the intolerance of pneumoperitoneum, the inability to achieve a correct working cavity, the failure of surgical instruments, or the expertise of the surgical team.

## 11.2 Technical Factors that Decrease Security

Cholecystectomy is a procedure that progresses with technical, systematized, and well-defined steps, involving prior theoretical knowledge and surgical skills. It is therefore important that the surgeon realizes when the dissection is becoming unsafe, the risk of injury, as well as the need to establish technical changes that will further lead the procedure to a correct outcome.

The impossibility of carrying on with surgery, anatomical disorientation, and decreased visualization, whatever the cause, are factors that take the procedure away from the safety path, increasing the risks.

There are factors that can affect the safety of a cholecystectomy; we can group them into anatomical, pathological, and technical factors.

The presence of inflammation, an impacted gallstone on the basin, or the impossibility of gallbladder traction affect the correct and safe identification and dissection of the hepatocystic triangle [4]. In order to maintain anatomical orientation as a safety element, several anatomical landmarks have been described, useful in cases where the hepatocystic triangle is not easily identified and that would allow anatomical-spatial reorientation in difficult cases, such as identifying the umbilical fissure or maintaining dissection above Rouviere's sulcus [5].

There are multiple anatomical variants of the bile duct and in relation to the upper biliary confluent, although between 53% and 63% of cases of their formation is modal [6]. Chaib [7] established five types of anatomical variants were characterized in the right liver duct (A1-5) and 6 types in the left liver duct (B1-6). Atypical branching patterns in both right and left liver ducts were found in 14% and 8%, respectively [7].

In our experience, the variation of the highest risk of bile injury is the abouchement of the right lateral duct (segments VI-VII) in the cystic duct (Fig. 11.1).

Regarding the ostium modalities of the cystic duct, they are also very variable; it can flow anywhere on the main bile duct, between CBS and Vater's ampulla [8].

Benson [9] described congenital anatomical variations of extrahepatic bile ducts and classified them in five main types, which are the most seen in surgical practice (Fig. 11.2).

In fact, only 33% of patients have the "classic" anatomical connection between cystic and extrahepatic bile ducts and related arteries, and in 75% of cases, the cystic has an angular input in the hepatic duct, which facilitates its identification and allows surgeons to describe the Calot's triangle [10].

In 20% of the cases, the cystic and hepatic duct come together in a long and parallel path, performing the actual abouchement further down the apparent junction, presenting a path attached in "shotgun pipe" [9, 11], which makes it difficult to identify the cystic duct and produces the bile injury.

In 5–8% of the cases, the cystic is tortuous and it can also be spiral shaped, describing variable entry angles in the common duct. The main bile duct can be surrounded from behind or front to flow to its left edge [11].

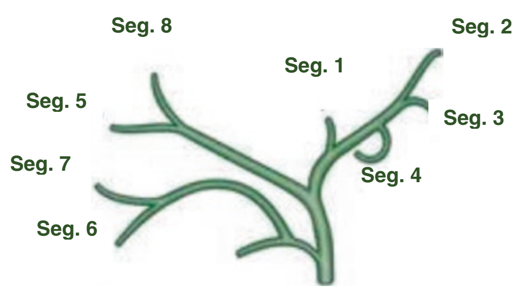


**Fig. 11.1** Right lateral sectoral duct ending into the cystic duct. (Courtesy of L. Ruso Martinez)

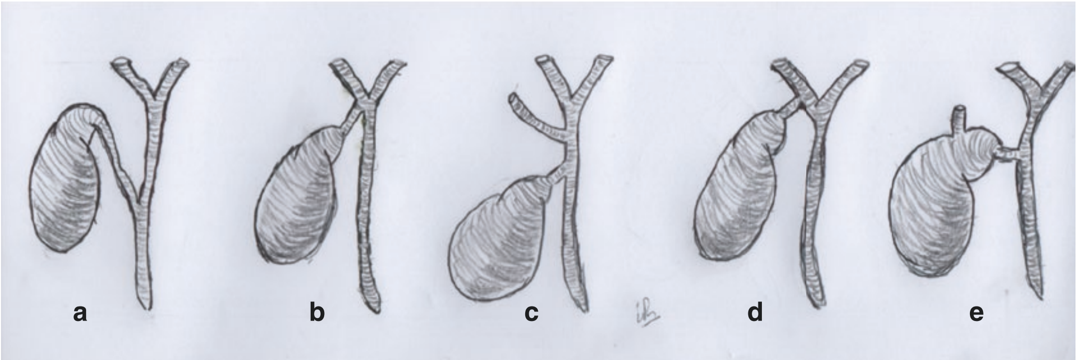


**Fig. 11.2** Benson-Page [9] classification for anatomical variations of the cystic duct insertion. (**a**) Long cystic with low insertion in the choledoco; (**b**) cystic ending in the superior biliary confluent; (**c**) right sectorial duct (seg VI-VII) ending close to the cystic end; (**d**) cystic ending in the right hepatic duct; (**e**) "Modal"cystic, ending in common bile duct. (Courtesy of L. Ruso Martinez)

There are pathologies and intraoperative findings that allow us to predict difficulties as they determine by different ways of limitations in the basic principles of a safe cholecystectomy.

Acute cholecystitis generates inflammation of the hepatocystic triangle, which in determining a limitation to CVS is one of the most common causes of tactic change. The presence of acute inflammation causes edema of the adipose cell tissue of the hepatocystic triangle, which can sometimes be a facilitating factor for dissection and anatomical identification, although in others it can easily bleed to contact, limiting it. Gangrenous cholecystitis with gallbladder wall necrosis is a determinant finding in the tactic because it limits the alternative possibilities to total cholecystectomy.

On the other hand, chronic inflammation is a determinant factor of scarring fibrosis at the hepatocystic triangle level. The presence of a complete scleroatrophic gallbladder causes the retraction and difficulty in the grasp; an impacted gallstone on the basin makes it impossible to dissect and display the structures. Mirizzi's syndrome and cholecystoenteric fistula that determine particular and specific anatomical alterations become a technical and tactical challenge, independently of the approach.

All these findings have something in common, the difficulty of getting a CVS (Table 11.1).

**Table 11.1** Intraoperative factors of technical difficulties

| |
|---|
| Thick wall gallbladder |
| Small gallbladder shrunken in the liver parenchyma |
| Chronicles/firm adhesions of the colon and duodenum in gallbladder bed |
| Cirrhotic liver |
| Misidentification of anatomical structures. Biliary and vascular variations |
| Permanent bleeding that decreases the vision of the operating field |
| Failure to progress dissection |
| Unreasonable dissection time |

## 11.3 Safety Factors

The safety factors that allow to continue with the total cholecystectomy procedure come up from the analysis and knowledge of the technical limitations of it.

### 11.3.1 Critical View of Safety

Currently the CVS is the paradigm for performing a safe cholecystectomy. Recent recommendations (IRCAD Y SAGES) assume that CVS and training are the most relevant technical factors for decreasing bile duct injury (BDI) and also suggest as technical alternatives, dissection of the neck, and subtotal cholecystectomy [3, 12, 13].

The CVS is not a technique but is the final vision that is achieved after the dissection of the hepatocystic area, which leaves the duct exposed and the cystic artery, prior to its clipping and section [14, 15].

To achieve the CVS, there are three requirements, well-known: the Calot's triangle must be thoroughly cleaned of fat and fibrous tissue by its anterior and posterior face; the lower part of the gallbladder must be separated from the liver bed (dissection of the cystic plate) so that, finally, only two structures are visible entering the gallbladder. It is not necessary to expose the bile duct. Once the critical security vision is obtained, the cystic structures can be connected [14, 16, 17].

The creation of two holes in the hepatocystic area does not ensure the CVS, until the region is completely dissected, on both sides, with the total circumferential vision of the duct and the cystic artery (double view). This allows a safe identification of a possible third abnormal structure (arterial or biliary) that needs to be preserved.

However, it is difficult sometimes to dissect the structures of the Calot's triangle; to accomplish this can take an excessive time and beyond the conviction of the surgeon who is observing the correct structures, the presence of a Mirizzi's syndrome, gallstones in the Hartmann's pouch that hid the cystic, and the main bile duct; also scarring fibrosis and acute inflammatory edema, the existence of epiploic block, abscess, gallbladder necrosis, or perforation may decrease the safety of the procedure [18].

Likewise, it is a prerequisite to understand the concept of CVS and to be convinced of its usefulness. Nijssen [19] in a recent report shows a review of video and operative notes of laparoscopic cholecystectomy that CVS was achieved in only 10.8% of cases, although it was reported that it was accomplished in 80% of the cases. In a survey of experienced surgeons from 14 Latin American countries, only 21.8% answered correctly to the definition of CVS [20]. In the Ircad [12] study, 76% of general surgeons and 96% of HPB surgeons consistently applied CVS.

Failure to achieve a CVS after a reasonable attempt and the existence of a difficult situation represent a high risk of injury. The CVS prevents injury from misinterpretation of the anatomy, but not by a direct injury as a result of continuing dissection in a hostile environment [14].

In short, safety in cholecystectomy is more complex than theoretical knowledge of CVS principles, since the necessary technical skills and maneuvers may require a level of training which exceeds the safety of the procedure.

### 11.3.2 Primary Dissection of the Gallbladder–Cystic Junction

In situations of difficulty, such as anatomical identification or when CVS is not achieved, the technical alternative may be the location and primary circumferential dissection of the gallbladder–cystic junction. It starts with the peritoneal section on both sides of the gallbladder basin and continues with blunt dissection from right to left, until an orifice is made at the level of the gallbladder cystic angle. That being stablished and based on the fact that the safe dissection plane is the gallbladder wall, the dissection is maintained through the subsequent plane to avoid vascular or biliary injuries, continuing along the inner edge of the gallbladder, ligating it in an upward direction.

A limitation is that occasionally the cystic artery transgresses the cyst or it is parallel to it, or behind, to end at the gallbladder cystic angle. In these cases, the artery is bound, the presence of the cystic is confirmed, and the dissection is continued upwardly.

This reverse alternative of the infundibular technique avoids the "tunnel effect" well described by Strasberg [21]. It does not require the dissection of the Calot's triangle or the visualization of the main biliary tract, as the dissection is maintained in the area of the hepatocystic ligament at the Hartmann's pouch [22].

### 11.3.3 Imageology

Getting a bile duct mapping in a difficult surgical environment can be hard, but it is a tool that allows cholecystectomy to continue more safely.

### 11.3.4 Intraoperative Cholangiography (IOC)

IOC is the most widely used method for the assessment of the bile duct in the intraoperative. While there is no conclusive evidence that the IOC prevents BDI, it is a recommended tool for defining an unclear anatomy during a difficult cholecystectomy [12]. It is a technique that can be performed in 90–95% of cholecystectomies, but in cases of short or thin cystics it can be particularly difficult. Cholecysto cholangiography through infundibular gallbladder opening and puncture or placement of a Foley catheter is a good alternative to achieve biliary opacification.

The limitations of it are that it must be technically well done, visualizing the entire biliary tract, intra and extrahepatic, and the passage of contrast to the duodenum, which involves knowing the biliary anatomy and its variations for a correct interpretation, and being performed without extending the surgical time too long.

Less routine use: Laparoscopic ultrasound. It allows the assessment of biliary and vascular pieces, arterial and venous, with the advantage of being noninvasive and radiation free, although it requires adequate training.

Also, near-infrared fluorescence angiography. Recently implemented, it is effective and safe in several studies, but its use is not yet widespread.

### 11.3.5 Surgical Time

Surgical time is an indicator itself of difficult cholecystectomy. It depends on multiple factors, such as surgeon skills, surgical team experience, and expertise.

The decision whether to continue with laparoscopy or not does not depend on a time factor but on the balance between difficulties in dissection progress, risks of complications, and extended surgical time.

The time for a change of surgical tactical (cholecystostomy/conversion) varies from 30 to 90 min depending on the experience of the surgical team, bleeding, patient tolerance, and complications.

In a multicenter study, 41% of surgeons consider that the maximum time for laparoscopic cholecystectomy should be 180 min, while 26% do not consider time as a determinant factor for conversion [23]. Recent reports conclude that more than the duration of the cholecystectomy is the experience that determines whether to continue laparoscopically or not [24].

### 11.3.6 Abstention to Continue

It is an attitude of prudence in the course of an uncertain dissection and/or in the presence of sustained unidentified structures. Therefore, three possibilities come up from this: performing maneuvers to increase vision and facilitate dissection, consult another surgeon or if this is not feasible, and the adoption of alternative techniques.

### 11.3.7 Maneuvers to Increase Visualization

They are made to improve visualization of the surgical field and to improve dissection. Gallbladder puncture and evacuation, very common in cases of thick-walled gallbladders, of difficult grasp or gallstones impacted on the basin; in that case, if it is feasible, the gallbladder opening and removal of the calculi to continue the procedure safely. Placing a fifth trocar, is a maneuver to keep in mind, as well as the suspension of the round ligament or conversion to assisted hand, a less frequent procedure that requires experience and suitable equipment for its performance.

### 11.3.8 Second Opinion

A second opinion consult to a more experienced surgeon or HPB surgery specialist is present in all published recommendations on this topic. In addition, up to 18% prevention of biliary/vascular injuries has been reported when calling a second surgeon because of unexpected findings [25].

### 11.3.9 Alternatives to Cholecystectomy

While the ideal objective is total cholecystectomy, in cases where the safety of the procedure is at risk, there is the option of alternative procedures that allow the treatment of the pathology without exposing the patient to a high risk of bile or vascular injuries. The clinical judgment of the surgeon is essential to define when a dissection becomes difficult and therefore risky and determines the need for alternative procedures, taking into account their experience and expertise.

### 11.3.10 Conversion

It is clear that the conversion does not guarantee the security of the procedure and therefore many times is not the solution to the problem. In fact it is a controversial issue among those who find that the conversion is associated to three times more complications, mortality, surgical site infection, hospital stay, and readmission than total laparoscopic surgery, while other authors show that there are eight times more bile duct injuries in unconverted patients [26, 27].

### 11.3.11 Percutaneous Cholecystostomy

It is a timeserver procedure that causes symptomatic relief until final resolution.

### 11.3.12 Partial or Subtotal Cholecystectomy

In the face of a frozen pedicle with intense fibrosis, subtotal cholecystectomy is an option, avoiding dissection in a risky area.

Ideally, lithiasis should be removed and then the cauterization of the remaining gallbladder must be performed. These procedures can be performed laparoscopically or after conversion, with the surgeon's experience being a determinant factor. An increase in incidence of bile fistulas in subtotal cholecystectomies has been reported, compared to total cholecystectomy (6.3% vs 0.35%), probably related to the incomplete closure of the residual infundibulum. However, morbidity is relatively low requiring endoscopic resolution between 1.5% and 15% [28]. In a review of 1231 subtotal cholecystectomies, of which 73% were laparoscopic, 0.3% postoperative hemorrhage was found, 2.9% sub hepatic collection, and 0.08% BDI [29]. Therefore, laparoscopic subtotal cholecystectomy is a valid and safe option to avoid BDI during a difficult cholecystectomy. Although with a high biliary leakage rate of 18% [29].

### 11.3.13 Anterograde Cholecystectomy Technique or Fundus First Cholecystectomy

This technique performed during the conventional procedure is also applicable to laparoscopic approach, but it requires a clear knowledge of the anatomy and cystic plate area and hilum to avoid injury [30]. In our experience, despite the fact that it appears in recommendations of recent publications [12, 13], we consider it a risky technique because the possibility of confusing the dissection planes next to the liver hilum.

### 11.3.14 When Is It Safe to Continue Laparoscopically?

When difficulties are checked during cholecystectomy, the surgeon should think calmly if the procedure should be carried on laparoscopically.

It is possible to continue laparoscopic surgery in the presence of objective safety indicators when:

– There is the conviction of the surgical team that there is proper exposure of the hepatocystic area and that the visceral tractions are made in a technically correct way.
– An appropriate CVS is established.
– Circumferential dissection of the gallbladder cystic angle is achieved, and the cystic artery is visualized, with double vision of both structures.
– There is no doubt regarding the safety of the ongoing surgical procedure.

This determines that no "no return" maneuvers should be performed that require cholecystectomy of necessity before deciding whether to do the procedure or not. In this situation, intraoperative cholangiography, correctly interpreted, showing the entire bile tree can enable us to continue with the procedure.

Finally, to continue with laparoscopy to the extent that the correct identification of the anatomical structures is achieved, this is the synthesis of dissection plus image in a rational time span.

Failure to progress dissection, whatever its cause, may be the determinant factor in adopting an alternative laparoscopic technique, such as subtotal cholecystectomy or cholecystostomy.

Conversion will be an alternative if the team has experience in open gallbladder surgery. Our consideration will be limited when such experience is exclusively, or almost, laparoscopic. Prior to the decision, the infrastructure conditions must be verified to see if they are in place to continue via laparotomy.

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# 12 Open Partial or Subtotal Cholecystectomy: Techniques and Indications

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## 12.1 Introduction

Laparoscopic cholecystectomy is the gold standard for gallstone disease [1]. Technical skills and learning curve are very important to reduce the risk of complications during the surgical procedure [2]. The complication most feared by surgeons is iatrogenic bile duct injury (BDI) which is associated with significant morbidity and mortality [3].

To reduce this complication, various measures have been proposed during laparoscopy: the use of a laparoscope at 30° and avoidance of tenting [4]; the use of a "critical vision" approach [5]; and the "dome-down" LC [6]. All these procedures have permitted to reduce BDI from 0.5% in 1990 to 0.3% in 2009 [7]. However, when the surgeon is not sure that he can manage the integrity of the biliary tract, the conversion to open surgery remains mandatory, especially in cases of difficult cholecystectomy as for acute cholecystitis [8].

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Even today conversion to open surgery is part of the laparoscopic cholecystectomy which is required for patient safety. The conversion rate is between 5% and 7%. The causes of conversion are severe inflammation (55.3%), adhesion (26.0%), bleeding (5.3%), probable choledocholithiasis (4.3%), and inability to continue (5.3%) [9].

In all these cases in which the structures of the Calot's triangle (cystic duct, cystic artery, common bile duct) cannot be identified in a safe manner, open subtotal cholecystectomy has proved to be a safe, simple, and definitive procedure [10].

A recent systematic review has shown that male patients, aged between 60 and 65 years, sclerotic gallbladder or wall thickness (4–5 mm), and acute cholecystitis are at most risks of surgical conversion [11].

## 12.2 History

In 1882, the open cholecystectomy technique was described [12]. This technique was considered the standard technique until 1987 when laparoscopic technique was reported for the first time [12].

Many changes were proposed after the first technical description for the management of the difficulties that may arise during both open and laparoscopic surgery. Those difficult conditions can be classified into five categories: adhesions with greater neovascularization, difficulty in treating the liver, inadequate exposure of the


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Calot's triangle, a high-risk gallbladder bed, and a high-risk hilum [13].

The first modified cholecystectomy was described by Hans Kehr in 1898 when he reported the case of a 27-year-old lady with acute cholecystitis who underwent surgery. He could not remove the hardened posterior wall of the gallbladder and its part close to the cystic duct because of the adhesions. So, he modified the traditional technique in order to avoid severe injuries. However, he also reported a severe postoperative bile fistula which required a further operation [14]. After the description of Kehr, several techniques have been described in order to manage difficult cases.

In 1938, Estes [15] advised performing a subtotal cholecystectomy when the level of inflammation was too high to make a clear identification of the cystic duct. A longitudinal incision was made along the gallbladder's wall up to 1–2 cm from the cystic duct, and the wall was swabbed with tincture of iodine. In this way, the removal of the impacted stones was possible. The redundant wall was trimmed, preserving the part attached to the liver bed. The cystic duct was not sutured, so there was no gallbladder remnant, and drains were placed [15].

In 1939, a technique was described which involved opening the gallbladder in the longitudinal direction, extraction of the stones, and the thermal ablation of both part of the wall of the gallbladder up to the sierosa which were sutured together to re-peritonealize the liver bed. This technique requires the suturing of the cystic duct and cystic artery as in total cholecystectomy [16].

In 1950, a variation of this technique was described. It contemplates the resection of the free wall of the gallbladder until the cystic duct. Since the cystic artery has to be sectioned at the inferior level of the gallbladder (within or on the wall of the gallbladder) near the cystic duct, it is recommended to suture the wall at the point to avoid vascular damages [17].

In 1954, McElmoyle [18] clearly illustrated his technique, underlying the difference with that one previously proposed by Pribram [19], Love [20], and Thorek [21]. In fact, these three authors advised to dissect and ligate artery and cystic duct and leaving a part of the gallbladder attached to the liver bed. Conversely, McElmoyle suggested that when it was safe, the dissection of the artery and cystic duct should be performed and associated with complete removal of the gallbladder wall. Otherwise, in difficult cases, the isolation of the artery and cystic duct should not be attempted, especially when there was not a visible surgical field. Consequently, the portion of gallbladder's wall closer to the important ducts and vessels was left in order to protect them from unsafe surgical maneuvers [18]. At the end of the McElmoyle's procedure, the edge of the remaining wall was sutured to control the bleedings, the mucosa was treated with phenol or electric cautery, and drains were placed [18]. Similarly to McElmoyle, other authors have supported the idea that it is safer to not close the cystic duct in order to avoid risky manipulations of the area [22].

Alternatively, a safe method is the closure of the cystic duct from inside by a purse-string as suggested by Bornman and Terblanche [23]. They also advised introducing a probe into a cystic duct for easier identification and ligation. However, the probe could be wrongly advanced in the common bile duct, especially if the cystic duct is short, leading to its erroneous ligation [24].

The Tokyo Guidelines 2018 [25] have summarized the technique of subtotal cholecystectomy, referring to the paper of Strasberg et al. [24]. According to this chapter, after emptying the gallbladder and cystic duct from stones and, eventually, a cholangiography or intraoperative ultrasound done, the posterior wall of the gallbladder is usually left in situ and ablated [25]. The ablation of the mucosa should minimize the recurrence of gallstones [26]. If there is a risk of bile duct injury (BDI), intraoperative cholangiography, intraoperative ultrasound, intraoperative indocyanine green fluorescence imaging may be useful, but there is no unified consensus on their usefulness. It is also possible a partial or total excision of the posterior wall but gangrenous gallbladder should be removed mandatorily. Oversewing the cut edges with a continuous suture is not mandatory but it could be helpful where the cystic artery branches reach the gallbladder, even if they are often thrombosed because of the inflammation. The suture from inside of the cystic duct is not compulsory but advisable. The number of drains depends on the degree of contamination. In the fenestrating subtotal cholecystectomy, the residual gallbladder lumen is open into the peritoneal cavity, while in the reconstituting one the lumen is closed with sutures or staplers [24].

## 12.3 Indication

Open conversion is required in 5–10% of cases with an increase in hospital days [38]. Between 0.2% and 1.1% of patients undergoing not converted laparoscopic difficult cholecystectomy reported bile duct lesions [27].

Open conversion is necessary in case of difficulty in identifying the bile duct, cystic duct, and cystic artery or in case of intraoperative complications (bile duct injury, hemorrhage, intestinal perforation, etc.).

In literature, several factors that can increase the possibility of converting into an open procedure are reported: age [28], male sex [29], obesity [30], cholecystitis [29], and ERCP [31].

The most common presentation of patients with acute cholecystitis is abdominal pain in the right hypochondrium, fever, and high white blood cells. The liver function tests can be normal.

During radiological examinations, it is possible to forecast the possibility to use the subtotal cholecystectomy technique. When the US or CT scan show a severe inflammation or complications as fluid collections or gas in the wall or the lumen of the gallbladder or free air in the peritoneum, an open technique with subtotal cholecystectomy can be necessary [10].

For this reason, many authors report scores to predict the possibility to convert to open surgery.

Sutcliffe et al. reporting CLOC score. This score is applicable before the laparoscopic surgery. Where a lower score $\leq 6$ is a low risk, so patients can be treated by surgeons in the first phase of training. A higher score $\geq 6$ is a high risk of conversion and the patient should be operated by experienced surgeons [32].

Sugrue et al. reported a 10-point intraoperative gallbladder scoring system (G10). The gallbladder surgery was considered easy if the G10 score $< 2$, moderate ($2 \leq 4$), difficult ($5 \leq 7$), and extreme ($8 \leq 10$). Conversion occurred in 33% of patients with G10 scores of $\geq 5$. Completely buried GB, impacted stone, bile or pus outside GB, and fistula represent the four factors statistically predictive of conversion [33].

In literature, two techniques are reported for open cholecystectomy in difficult gallbladder: partial cholecystectomy and subtotal cholecystectomy. The difference between partial and subtotal cholecystectomy is not well explained in the literature because many authors have used the term partial and subtotal in a personal way. Partial should mean the removal of part of an organ while the subtotal should mean the removal of almost all of an organ.

Some authors suggest using the term subtotal to indicate the extent of the resection. If it is removed only upper part can be used the term fundectomy and eliminated the term partial [24].

## 12.4 Technique

The open techniques to remove gall bladder are summarized in three categories: the first reports to leave the cystic duct closed with clips or inside the Hartmann's suture bag and leaving the posterior mucosa adherent to the liver; the second technique reports to leave the cystic duct and the Hartmann's bag left open and drained; the third technique contemplates leaving the cystic duct open and the Hartmann's bag closed with stapler or suture [34].

The technique for subtotal cholecystectomy used by the authors is the following: a small right subcostal transverse incision (max 12 cm) is performed under general anesthesia (Fig. 12.1). After the gallbladder is incised by electrocautery at the fundus, the bile or pus is aspirated (Fig. 12.2a, b) and the stones evacuated. Then the fundus of the gallbladder are resected, and the anterior wall is transected until 1 cm before the cystic orifice in order to visualize it (Fig. 12.3). At this moment,

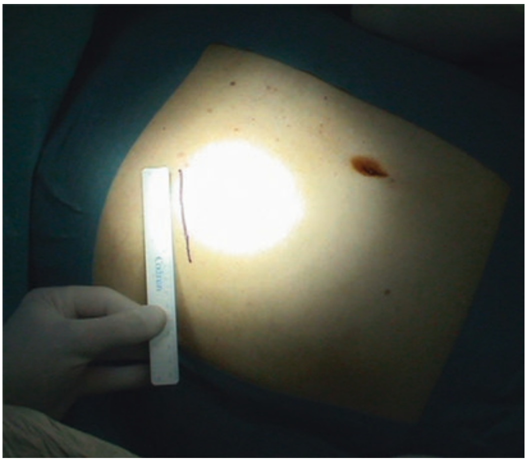

**Fig. 12.1** Skin incision up to 12 cm. (median incision is 8 cm)

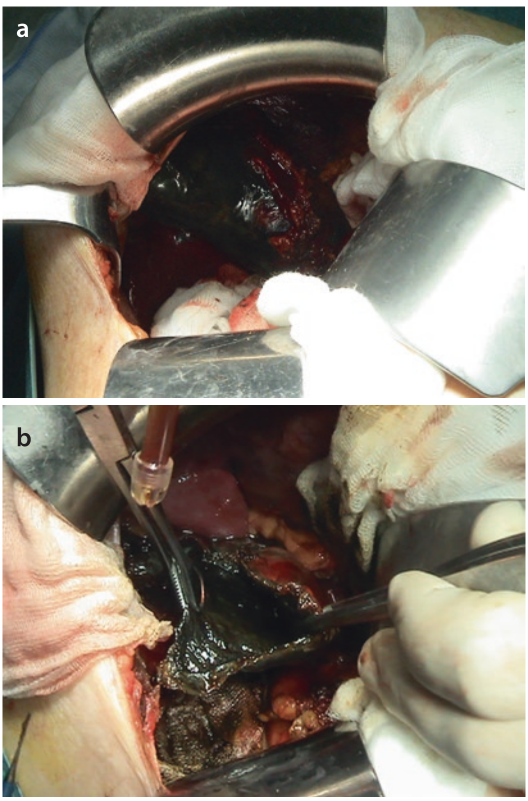


**Fig. 12.2** (a) Intraoperative view of cholecystitis (b) The fundus is incised and resected, then the gallbladder is empty of all contest (bile, pus, stones)

the posterior wall is resected from the liver bed (also this, 1 cm before the cystic orifice). The remaining anterior and posterior infundibular tis-

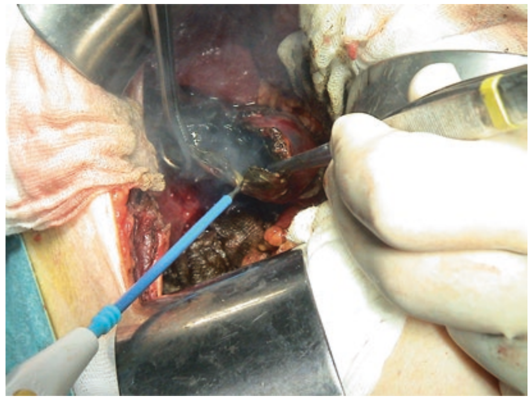

**Fig. 12.3** Resection of anterior wall until the cystic orifice

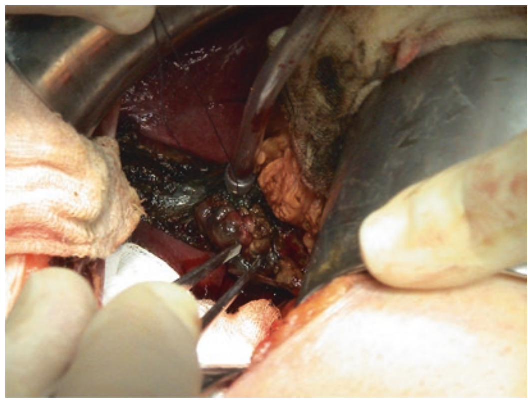

**Fig. 12.4** Remaining infundibular anterior and posterior wall are sutured in order to safely avoid CBD lesion and to eliminate any residual cavity in the infundibulum

sue is closed hermetically by double running suture in order to avoid bile leakage or, more important, the formation of a new cavity [10] (Fig. 12.4). A small drainage can be left in place depending from the intraoperative situation.

It is described by many authors how the anterior wall of the inferior infundibulum should be sutured to the posterior wall left adherent to the liver bed, but this difficult technique could create a new cavity and be the origin for stones recurrence. Furthermore, performing this suture, it is possible to damage the hepatic parenchyma causing bleeding.

When a high grade of inflammation is present, the limits between seromuscularis tissue and mucosa are hard to be individuated. For this reason, in this case, it could be much cautious leaving in place the posterior wall of the gallbladder leaving open the cystic orifice.

Furthermore, the risk of a suture only with the mucosa can consequently create a subtle infundibulum wall that can be damaged by the traction practiced during the suture and causes necrotic degeneration or fistulas. This is why the technique of suturing the anterior wall to the posterior wall has to be practiced only when this last is separated from the liver bed, in order to create a stable structure with no risk of new biliary cavities [10].

## 12.5 Complications

During subtotal cholecystectomy, the dissection and ligation of the cystic duct is difficult, but needed, by some authors, to avoid a postoperative bile leakage [34].

Furthermore, patients undergoing subtotal cholecystectomy have a higher rate of biliary fistula, an overall increase in length of hospital stay with an additional cost due to ERCP, and biliary stenting. But debate is still open because the low incidence of biliary fistula and effective treatment with ERCP reduce morbidity and do not justify to exploration of the common bile duct or more difficult procedure to tie the cystic duct [35].

The use a 10 French endoprosthesis in the cystic duct stump to allow the complete closure of the persistent fistula in 6 weeks is reported in the literature, but is not commonly used [36].

Other authors show a technique in which a piece of omentum is plugged into the gallbladder stump to avoid bile leakage. This technique is used when it is not possible to close the cystic duct due to a difficult gallbladder [37]. Also, this technique is not commonly used.

The closure of the residual gallbladder (Hartmann's pocket) can be considered the safest method, but if not well performed it can cause the formation of the gallbladder residue which reduces the incidence of biliary fistula but in which the formation of the bile stones is possible [38]. In literature, there are no indications on the incidence of symptomatic residual gallbladder after subtotal or partial cholecystectomy because there is no long follow-up, and the residual gallbladder can give clinical signs after many years of surgical treatment [38]. In the cases of the patients with residual gallbladder can be necessary a new surgical procedure to remove the residual gallbladder [24].

The advantages of subtotal cholecystectomy are the reduction of recurrent gallstone formation because all the gallbladder mucosa is eliminated and the necrotic parts of the gallbladder are removed, avoiding the formation of empyema [35].

The disadvantages of subtotal cholecystectomy reported in the literature are the increased incidence of infection and intra-abdominal injury [35], cystic stump syndrome (continuous discharge of mucus from the retained gallbladder mucosa), subphrenic collections, or persistent drainage from the drainage site [39].

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# 13 Laparoscopic Subtotal Cholecystectomy and Other Laparoscopic Techniques

Elena Schembari, Maurizio Mannino, Adriana Toro, Piero Marco Fisichella, and Isidoro Di Carlo

## 13.1 Introduction

When laparoscopic cholecystectomy (LC) is difficult due to a severe inflammation degree that makes the Calot's triangle dissection challenging, conversion to open surgery was suggested in the past. Nowadays, thanks to the increasing surgeons' laparoscopic experience, several tricks have been described to have a better visualization of the operative field in order to finalize the total cholecystectomy by laparoscopy. Moreover, when a "critical view of safety" (CVS) is not possible, other laparoscopic techniques have been advised to manage the difficult cases that can be treated by subtotal cholecystectomy or other techniques that do not resect the gallbladder in its entirety but leave a part of the gallbladder wall in place. This chapter will explore all these possible solutions and suggest that a change in surgical laparoscopic strategy can give better results than the open conversion.

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## 13.2 Tricks

Many tricks have been reported in literature to make a cholecystectomy easier. Santos et al. [1] described the trocars' position in obese patients. The camera trocar should not be inserted at the umbilicus but 15 cm below the xiphoid process. The reason is that in these patients the umbilicus is located lower in the abdomen, and consequently the placement of the camera trocar in this site would make more distant and difficult the visualization of the gallbladder. Even previous median laparotomies are contraindications for umbilical access; in these cases, the first trocar should be placed in the upper left or right quadrant in order to remove adhesions in the umbilical region and allowing a safe insertion of the camera trocar.

Moreover, in obese patients with a substantial amount of intra-abdominal fat and the omentum covering the gallbladder, the traditional reverse Trendelenburg position slightly turned on the left side could not be enough to achieve a good visualization of the gallbladder and an instrument should be used to take them away from the surgical field.

In addition, the use of a further 5 mm trocar should be considered as a valid option for facilitating the surgeon's performance as for bulky left lobe of the liver that can be found not only in obese patients but also in normal weight subjects.


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A 30° or 45° laparoscope should be preferred to a 0° one because this facilitates the vision during the lateral and medial dissections.

Decompression of gallbladder by needle aspiration is advised when its distension is too exaggerated and interferes with the field of view [2].

During the dissection, the intensity of diathermy should be regulated according to the size of the patient and the surgeon's skills. High levels of energy can not only damage closer organs such as duodenum and stomach during adhesiolysis but also burn the liver with possible postoperative bile leakages. Undoubtedly, modern energy devices (Harmonic, Thunderbeat) facilitate the hemostasis in patients with acute cholecystitis or cirrhosis, even if there are some risks of serious injuries due to the thermal spread [1]. Persistent mild bleedings should be managed by compression, while uncontrolled clipping and electrocautery should be avoided [2].

Another fundamental step during the dissection is the correct exposure of the Calot's triangle. An adequate retraction of the infundibulum towards the lateral and caudal parts of the patient allows the opening of the triangle. Without this maneuver, the cystic duct would lay parallel to the common bile duct and distinguishing these two structures could be challenging, with an obvious increased risk of damaging the common bile duct. The assistant could make this phase easier, facilitating the visualization of the infundibulum by pulling up and to the right patient's shoulder the fundus of the gallbladder. Moreover, thanks to this maneuver, the incision of the medial peritoneal attachment of the gallbladder can be safely performed. This in conjunction with the lateral attachment incision will result in a further opening of the Calot's triangle and give access to gallbladder's wall through the inflammatory capsule [1].

When the cystic artery is short or enters high into the gallbladder, it hinders a reliable achievement of CVS. In such occasions, it has been advised to cut it. The aim of this procedure is to allow clear visualization of the cystic duct which will be the only tubular structure in the Calot's triangle. However, before performing this division, the surgeon must be sure that the identified structure is the cystic artery. This represents a crucial step because, basing this assessment just on the presence of pulsation or its size, the cystic artery could be confused with the right hepatic artery or with the cystic duct. In order to avoid this unpleasant and dangerous misidentification, removing all the tissue (such as fat) which surrounds the cystic artery is fundamental, and this vascular structure should be followed from its origin to its entrance into the gallbladder [3].

However, surgical decision-making remains the most fundamental element in the management of difficult cholecystectomy [4]. Unclear anatomy, bleedings, bile leakage, and the use of several clips are all factors that should encourage the young surgeon to ask for some help. Converting to open cholecystectomy can be useful to get out of Dodge, but it is not always the best solution to make a cholecystectomy easier. In fact, having the opinion of a colleague with good expertise in laparoscopic surgery can be more effective rather than converting to open surgery. Moreover, there are other strategies that can be used to overcome these difficult situations because the safety of patients has to ever guide the surgeon's behavior.

## 13.3 Alternative Strategies

The surgeon should always bear in mind that cholecystectomy is usually performed for benign disease [4]. Dangerous maneuvers, which can lead to serious injuries and sometimes life-threating situations, should not be carried out especially because there are other solutions that are safe and effective. So, the decision of changing the surgical strategy should be made before doing vascular or biliary injuries.

The CVS is not the only technique to isolate the cystic duct, but the infundibular technique could be also adopted (Fig. 13.1). According to this method, the dissection of the cystic duct is made on the front and back of the Calot's triangle once the cystic duct is found, and it is traced on to the union with the gallbladder. A typical flare or funnel shape is evident when the cystic duct joins the gallbladder. However, this technique seems to

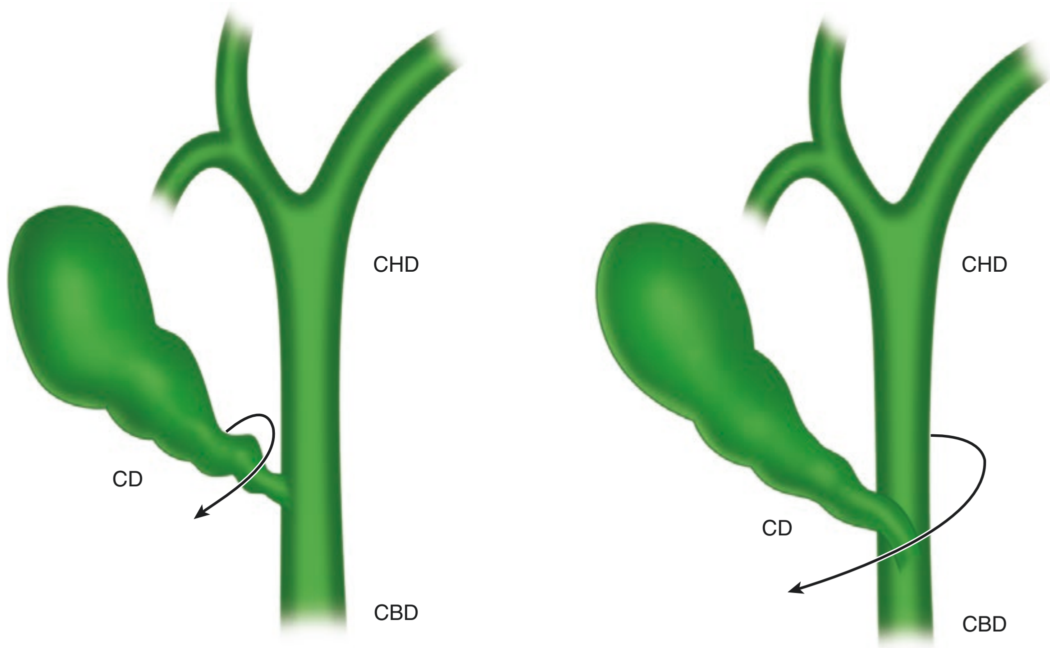


**Fig. 13.1** The infundibular technique of laparoscopic cholecystectomy. Left: typical anatomy, where the dissection is made around the cystic duct (CD), which can be easily distinguished and is far away from the common hepatic duct (CHD) and the common bile duct (CBD). Right: due to the inflammatory process, the CHD could be adherent to the CD and misidentified as this. So, the circular dissection is more likely to be wrongly made around the block CBD–CD rather than just around the CD, causing biliary injuries

create a flaw in the visualization of the cystic duct. In fact, it has been demonstrated that, in case of severe inflammation, it is hidden, and the risk of misidentifying the common bile duct as the cystic duct and biliary injury is high. In these situations, the dissection around the left and the right sides of the common bile duct instead of anteriorly and posteriorly to the Calot's triangle can be done but very cautiously and only in expert hands. As a result, this technique is unreliable, even if it is performed by expert surgeons, and should be avoided [5].

In 1994, LC from "fundus downward" or "fundus first" was proposed by Kato et al. [6]. When the exposure of the cystic duct was difficult, the gallbladder dissection should start from the fundus and the cystic duct should be clipped and cut at the end of the procedure. This technique was slightly modified by Uyama et al. [7], who lifted the liver bed up to the diaphragm by a suture, obtaining a good view of the operative field. However, because of the contraction of the Calot's triangle occurring during an inflammatory process, the lower end of the gallbladder becomes closer to the common hepatic duct, the right hepatic artery, and the right or main portal veins. So, gallbladder and common hepatic duct can be perceived by the surgeon as one structure, the route of the dissection will be wrong, and, at the end of the procedure, the common hepatic duct will be divided [8].

The impossibility of obtaining a CVS is a clear signal that a bailout procedure should be considered [2]. Thanks to a subtotal cholecystectomy (SC), it is possible to treat the disease at once, avoiding a second operation. Indeed, subtotal cholecystectomy in the case of portal hypertension or cholecystitis is a well-known technique [9]. Generally speaking, "subtotal" means almost complete removal of an organ, while "partial" refers to the removal of a portion of an organ. These two terms have been used in literature to describe the same extension of an incomplete gallbladder resection. However, Strasberg [10] suggested that the term "subtotal" was more accurate to describe this type of surgical procedure and avoid confusion. The term "fundectomy" should be adopted referring to the removal of the top part of the gallbladder. As a result, the word "partial" should not be used anymore. Furthermore, the terms "reconstituting" and "fenestrating" refer to the presence or absence of a gallbladder remnant that in the majority of cases concerns the posterior wall. The remaining portion of the gallbladder wall can be left open or closed, when it is sutured this has to be done as close as possible to the cystic duct. Otherwise the residual sutured stump, called "remnant," will result in a new and smaller gallbladder.

Overall, some differences come to light when the articles about subtotal cholecystectomy are examined. In fact, the authors of the published articles have controversial opinions about how to perform some steps of this procedure.

One of the most critical steps of the subtotal cholecystectomy is the handling of the cystic duct. Some authors prefer to isolate and close the cystic duct with surgical clips, suture ligation, Endoloop (Ethicon), purse-string suture, or intracorporeal sutures for closure [11, 12].

Palanivelu et al. [13] introduced the concept of tailored subtotal cholecystectomy by laparoscopy. In fact, they classified laparoscopic subtotal cholecystectomy (LSC) in three types which were performed according to the risk of damaging liver bed or hilum. So, in type I, they suggested to not remove the posterior wall of the gallbladder when its dissection from the liver bed was difficult for an increased risk of bleeding. The remnant mucosa could be removed (mucosectomy) or electrofulgurated. Type II should be performed when recognizing the hilar structures was complicate, the entire gallbladder was removed, and the infundibulum was cut close to the cystic duct and sutured with a continuous suture of polyglactin 3–0. Finally, when high-risk hilum and gallbladder bed coexisted, a combination of LSC I and II should be performed and this was called LSC III.

When LSC is performed, there are two possible options to manage the remnant gallbladder stump. The first option is to close it, reconstituting the gallbladder as in open surgery described by Strasberg. Several methods can be used to do it like an absorbable suture [14], a purse-string suture [11], endoloop [15], or an EndoGIA stapler [12]. All these techniques have to be used carefully, and they can be applied only when a safe distance between the cystic duct and the common bile ducts exists. Otherwise, the risk is to have the traction and consequently involvement of the CBD and all related immediate or late complications. This closure can be performed also when the posterior wall of the gallbladder is not excised [10]; in this case, it is completely cauterized with the only exception of the part that will be sutured. The second option is to leave it open (fenestrating LSC), closing the cystic duct [16, 17] or leaving it open. Drains are usually placed [18, 19].

Recently, the association of "fundus first" LC and subtotal cholecystectomy has been proposed [20, 21]. According to Harilingam et al. [20], the procedure starts with the opening of the fundus to drain its content (pus, bile, stones). After dividing the gallbladder into two halves, the posterior wall is used to make traction and pulling up the liver and the anterior wall is transected at the level of Hartmann's pouch. Then, the posterior wall is divided from the liver bed, but, when this dissection is difficult, it is cauterized. The cystic duct or the small gallbladder remnant is closed with an intracorporeal stitch or endoloop. The rationale of this technique is that viewing the gallbladder from the inside could make the dissection safe, reducing the risk of biliary and vascular injuries. Moreover, an intraoperative cholangiography could be performed. Nasr et al. [21] proposed the traditional fundus first technique, but they ended the dissection at the so-called "Critical Point of Surgical Control" (CPSC) of the gallbladder. The CPSC is the junction between the gallbladder neck and the cystic duct where the cystic artery comes into the gallbladder. When they arrived at CPSC, an endoloop was applied to control the hilum of the gallbladder. However, due to the small number of patients involved in these studies [20, 21], it is not possible to conclude if these techniques have better outcomes than the others [2].

## 13.4 Outcomes

Overall, postoperative bile leakage was more frequent after laparoscopic subtotal cholecystectomy compared with open conversion, while rates of retained stones, subhepatic collections, wound infections, reoperations and mortality were all lower [22]. Moreover, the incidence of postoperative complications after subtotal cholecystectomy (SC) is similar to that after a total cholecystectomy (TC) and, taking into account that SC is usually performed in difficult cases, this means that SC is a safe and simple method to manage complex situations. It is important to highlight the lower rate of common bile duct injury after SC rather than TC, which is one of the most important reasons why the SC is performed because it avoids hazardous maneuvers in the Calot's triangle [22]. In fact, vascular injuries can cause acute liver failure, while biliary obstruction dues to the wrong closure of the CBD could lead to secondary biliary cirrhosis and chronic liver failure. In both cases, liver transplantation is the only treatment [23, 24].

The most common complication of LSC is bile leak, which varies from 10.6% [25] to 18% [22]. This incidence is higher after laparoscopy maybe because the cystic duct (CD) can be closed with a tighter knot during an open procedure. The increased rate of bilomas and bile leaks after SC can be consequent to the inflammation because, when the inflammatory process is resolved, the edema disappears and the sutures used to close CD or Hartmann's pouch can become looser [22]. Bile leaks are more common when CD or Hartmann's pouch is left open rather than when they are closed [22, 25]. Leaving drainages in place is useful to monitor the evolution of the leakage also because the majority of bile fistulas can resolve spontaneously [22]. Otherwise, percutaneous drainage or ERCP can be used to address the problem [25].

The fundus-down technique is associated with a high incidence of vasculo-biliary injury, especially in difficult cases like severe inflammation with the fusion of the structures because it is easier to misidentify the correct plane [26]. For this reason, performing the dissection close to the gallbladder has been advised [2].

The incidence of recurrent or residual gallstones after intentional incomplete cholecystectomy has been estimated between 0.0% and 16% [18, 27]. During SC, stones placed in the gallbladder stump or cystic duct could not be identified, this could explain the increased incidence of retained stones after SC than TC. The difference in the rate of this complication is not statistically significant between cystic duct/gallbladder stump open and close, even if this appears to be slightly higher when cystic duct/gallbladder stump is left open [22]. In long-term follow-up, recurrent symptomatic stones can form in the gallbladder remnant in only 5% of patients, giving symptoms of cholecystolithiasis [2, 10, 25]. There is no evidence that increasing the number of LSC and reducing laparotomic conversions causes a rise in the rate of residual or recurrent gallstones. The size of the remnant could influence the probability of stone formation. Gallstones relapse is more possible if a "fundectomy" is done instead of a true subtotal cholecystectomy [28]. According to the intraoperative findings that some symptomatic gallbladder remnants had an internal diameter of only about 1 cm, the section during an SLC should be performed very close to the cystic duct [10, 29]. Gallstones recurrence is a complication that a surgeon should consider in patients with symptoms related to biliary colic after an SC. Diagnosis of stone recurrence in a gallbladder remnant is quite complex, and it arises mainly from ultrasonography (US), computed tomography (CT), magnetic resonance cholangiopancreatography (MRCP), endoscopic retrograde cholangiopancreatography (ERCP) (which is also useful to treat residual gallstones of the common bile duct), and endoscopic ultrasonography (EUS). The surgical treatment represents the best option. The laparoscopic approach should be performed by expert surgeons because of the scar around the Calot's triangle following the previous operation [27, 28].

One of the disadvantages of LSC is that in the case of cancer that has not diagnosed preoperatively, there is the risk of tumor dissemination in the abdominal cavity and remnant tumors. A tumor should be excluded before surgery [30], even if the unexpected rate of gallbladder cancer has been reported to be very low, around 0.2–0.8% [31].

## 13.5 Conclusions

Severe inflammation could make LC difficult with an increased risk of vasculo-biliary injuries. A bailout procedure should be adopted when a CVS cannot be achieved because of severe fibrosis which hides the structures of the Calot's triangle. To avoid these damages, several rescue procedures have been proposed over time but only a few have been recommended. The first one is the laparoscopic subtotal cholecystectomy. This is superior to open conversion and TC in terms of postoperative complications and biliary injuries. So, SLC is a procedure that should be definitively considered in difficult situations. Conversely, there is no clear evidence about the safety of the fundus first technique even when it is combined with SLC. The open conversion is a controversial issue because the decision to convert into open depends on the surgeon's experience [2]. Most surgeons trained in the past 20 years have little experience in open cholecystectomy [8], so open conversion does not make surgery easier. Otherwise, open conversion does not exclude the opportunity to perform an SC when the intraoperative findings discourage a TC [2].

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# 14 The Indocyanine Green Role in Acute Cholecystitis

Rene Aleman, Fernando Dip, Emanuele Lo Menzo, and Raul J. Rosenthal

**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

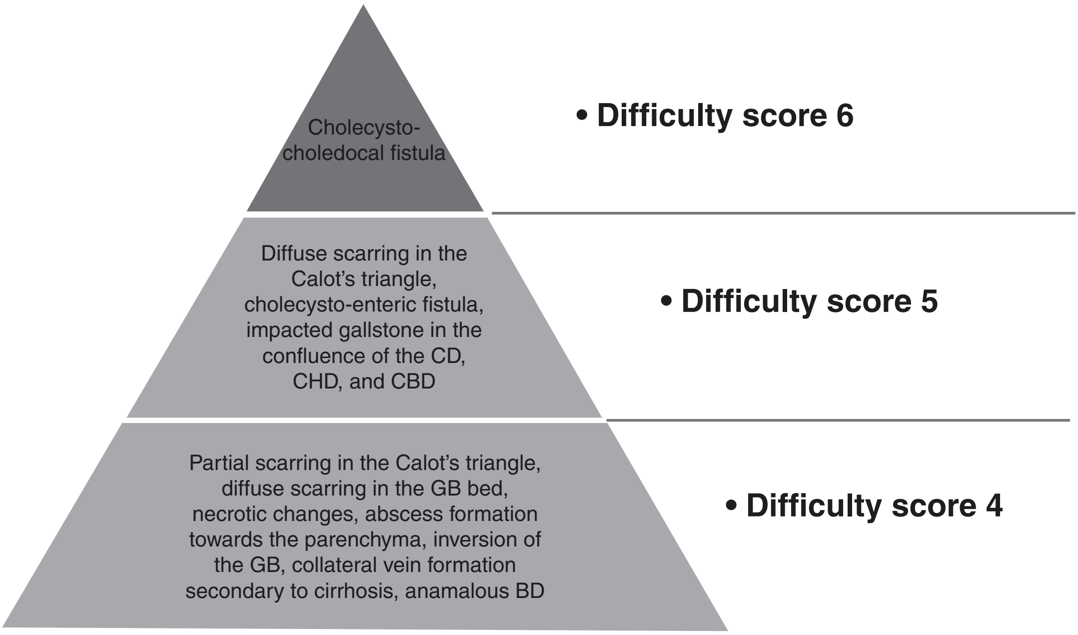



**Fig. 14.1** Most commonly encountered difficulty indicators during LC

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*<br>If a distended GB interferes with the field of view, decompress by needle aspiration | *Step 1*<br>Administration of peripheral ICG |
| *Step 2*<br>Effective retraction of the GB to develop a plane in the Calot's triangle area and identify its boundaries | *Step 2*<br>Exposure of the hepatoduodenal ligament |
| *Step 3*<br>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*<br>Initial anatomical evaluation: Identification of the biliary tree structures following lysis of adhesions |
| *Step 4*<br>Maintaining the plane of dissection on the GB surface throughout the procedure | *Step 4*<br>Identification of the CD and CBD junction |
| *Step 5*<br>Dissecting the lower part of the GB (at least one-third) to obtain the critical view of safety (CVS) | *Step 5*<br>Identification of the CD and its junction to the GB |
| *Step 6*<br>Creating the CVS | *Step 6*<br>Identification of the CHD |
| | *Step 7*<br>Identification of the CBD |
| | *Step 8*<br>Identification of the cystic artery and optional performance of an arteriography |
| | *Step 9*<br>Time-out before transection and reidentification of Calot's triangle structures |
| | *Step 10*<br>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**

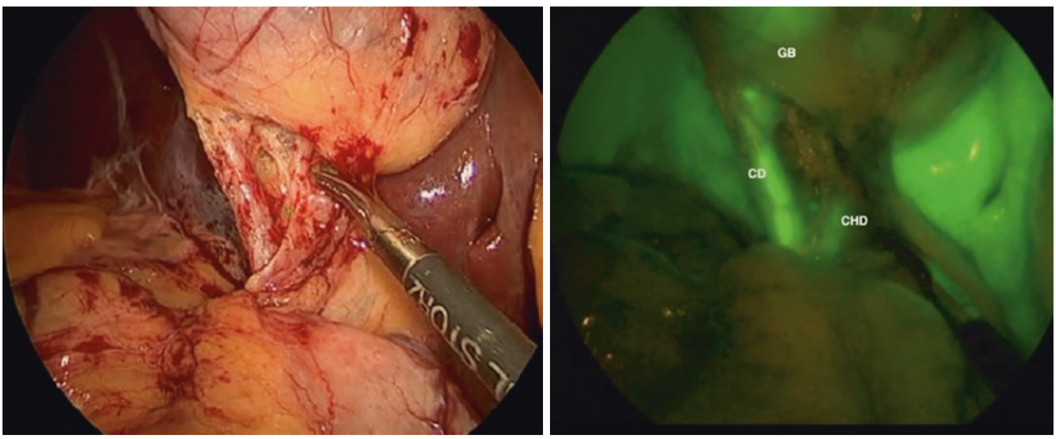
- Cephalad retraction of the GB to ensure complete view of the biliary tree anatomy - appropriate CVS.
- Prioritize on the dissection around the GB -if it is too dificult to procede, consider bail-out procedures.

**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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# 15 How to Avoid Common Bile Duct Injuries and Their Classification

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## Abbreviations

| | |
|---|---|
| BDI | Bile duct injuries |
| CBD | Common bile duct |
| CHD | Common hepatic duct |
| CVS | Critical view of safety |
| ERCP | Endoscopic retrograde cholangiopancreatography |
| ICG | Indocyanine green; |
| IOC | Intraoperative cholangiography |
| IOUS | Intraoperative ultrasonography |
| LC | Laparoscopic cholecystectomy |
| PTC | Percutaneous transhepatic cholangiography |
| RHD | Right hepatic duct |

## 15.1 Introduction

Laparoscopic cholecystectomy has become the gold standard for the management of symptomatic cholelithiasis and other gallbladder diseases. However, several reports demonstrated that the incidence of bile duct injuries (BDI) has risen from 0.2–0.3% in the era of conventional open cholecystectomy to 0.5–0.8% in the era of laparoscopic cholecystectomy [1–4]. Wrong or incomplete dissection of Calot's triangle, especially in cases of significant inflammation at the surgical site, or aberrant anatomy of the bile duct may result in bile duct injuries (BDI) [5, 6]. Iatrogenic BDI are associated with significant postoperative morbidity and mortality, decreased long-term survival, and quality of life and their management constitute a surgical challenge. The goal in these cases is the restoration of the biliary tree and the prevention of complications such as strictures, recurrent cholangitis and secondary biliary cirrhosis, abscess, and fistulae. Management depends on the timing of recognition of injury, the extent of bile duct injury, the patient's condition, and the availability of experienced hepatobiliary surgeons. Technical difficulty of repair, operative risk, and long-term outcome of bile duct injuries vary considerably and are mainly associated with the location and the extent of the injury. Consequently, several classifications with therapeutic and prognostic implications have been established [1–4]. However, as the precise causes of injury are becoming better understood, technical refinements for prevention are emerging. Prevention should be the goal and this requires adherence to strict principles of meticulous and safe dissection of the identified structures.

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## 15.2 Risk Factors for Biliary Injury

There are many factors that increase the incidence of BDI during laparoscopic cholecystectomy. First of all, the camera provides a monocular view from a direction quite different from that of open surgery, thus the CBD is not usually seen from this angle. The high rate of biliary injury in early reports was due in part to inexperience in the procedure. This was called the "learning curve" effect [7]. Indeed, experience contributes to BDI, but several other factors are responsible, as well.

Biliary injuries are more likely to occur during difficult laparoscopic cholecystectomies [8, 9]. The incidence of BDI when laparoscopic cholecystectomy is performed for acute cholecystitis (0.51%) was reported to be three times higher than that for elective laparoscopic cholecystectomy and twice as high as that for open cholecystectomy for acute cholecystitis [9, 10]. Severity of coexisting inflammation in the operating field with dense scarring contribute as well to intraoperative bleeding that obscures the field. Furthermore, the presence of abundant adipose tissue around the hepatoduodenal ligament, especially in obese patients, increases the difficulty of surgery and promotes BDI. Adverse factors include higher age (>65 years), male gender, morbid obesity and long duration of symptoms prior to surgery, upper abdominal surgery, history of attacks of acute cholecystitis, or previously established cholecystostomy [10].

Aberrant anatomy or anatomic variants and anomalies undoubtedly contribute to biliary injuries. The aberrant right hepatic duct anomaly is the most common problem because the duct may be mistakenly regarded as the cystic duct and ligated or cut. Excessive, more than is necessary, dissection around the hepatoduodenal ligament during cholecystectomy may lead to damage to the axial arteries running along the CBD. Vascular damage is the cause of postoperative biliary strictures due to ischemia.

Last but not least, maintenance of laparoscopic equipment is of paramount importance. Focal loss of insulation on electrocautery instruments may lead to thermal injuries [6].

## 15.3 Prevention of Bile Duct Injuries

Laparoscopic cholecystectomy is performed in an area adjacent to many vital structures such as the portal vein, hepatic artery, and extrahepatic biliary tract, and thus, thorough knowledge of the relevant anatomy as is of paramount importance for a safe procedure. The surgeon should be aware of anatomical variations and the anatomical distortion due to acute or chronic inflammation.

A number of factors predictive of difficult cholecystectomy have been universally recognized and should be identified in both acute cholecystitis and elective cases. The presence of these risk factors should alert surgeons with limited experience, for careful patient selection. On the other hand, the experienced surgeon should be prepared for the possibility of conversion to an open cholecystectomy, or need for various bailout procedures, such as the establishment of a tube cholecystectomy, subtotal or fundus first cholecystectomy, either laparoscopic or open [10–12]. The exposure and cautious dissection of Calot's triangle with judicious use of energy and meticulous attention to technique in order to achieve "the critical view of safety (CVS)" is an essential step of laparoscopic cholecystectomy.

It is important for the operating surgeon to be able to recognize when the dissection is becoming unsafe with a high potential for BDI. More than two tubular structures entering the gallbladder, unusually large presumed cystic artery or artery pulsations behind the presumed cystic duct which cannot be occluded with medium–large clips and is surrounded by excessive fibrofatty tissue, bile leakage with intact gallbladder, and/or bleeding requiring blood transfusion, are important indicators of unsafe dissection [10–14]. In such cases, the dissection should be stopped temporarily and reconsider alternative technical plans for a safe dissection, seek for a second opinion from another surgeon, preferably an experienced one. Various intraoperative imaging techniques, such as intraoperative cholangiography (IOC), laparoscopic ultrasound, and near-infrared fluorescent cholangiography, may be used to assess the biliary anatomy, as well [10, 13, 14]. Intraoperative team communication is obviously significant but the surgeon should know when to call for help and recognize the need for conversion or an alternative procedure, such as subtotal cholecystectomy [15]. However, converting to an open procedure does not safeguard against BDI (Table 15.1).

**Table 15.1** Essential steps to reduce BDI during laparoscopic cholecystectomy

| |
|---|
| Preoperative evaluation of predictors of a difficult cholecystectomy [male gender, obesity, age >65 years, previous attacks of biliary colic, increased interval between onset and presentation (>72–96 h), upper abdominal surgery, prior attempted cholecystectomy, fever, high ASA score, raised CRP and white blood cell count, thickened gallbladder wall (>5 mm), small contracted or distended gallbladder with impacted stone, cirrhosis etc] |
| Use an angled ($30^0$ or $45^0$) laparoscope |
| Use high-quality imaging equipment |
| Cooperation with a dedicated and experiences assistant |
| Application of appropriate lateral traction of the fundus |
| Use Rouviere's sulcus and the base of segment IV as landmarks to aid orientation |
| Dissection and correct exposure of the Calot's triangle end establishment of CVS: (a) hepatocystic triangle is cleared of fat and fibrous tissues; (b) the lower one-third of the gallbladder is separated from the liver to expose the cystic plate; (c) two and only two structures should be seen entering in the gallbladder |
| Judicious use of energy devices at Calot's triangle |
| Dissection of the liver bed along the cystic plate |
| Avoid dissection on the left side of the hepatoduodenal ligament |
| Knowledge of anatomical variations, both biliary and vascular<br>Early recognition if dissection becomes unsafe<br>Seek a second opinion from another surgeon I difficult or unexpected situations |
| Use of intraoperative imaging when the anatomy is not clarified; obtain intraoperative cholangiograms, liberally |
| Implement bail-out procedures, such as subtotal cholecystectomy, or fundus-first cholecystectomy in cases of severe inflammation and/or inability to perform CVS |
| Do not hesitate to convert to open cholecystectomy in cases where CVS cannot be achieved and bail-out strategies could not be implemented |

Adaptation of well-proven principles of open surgery is the best prevention of biliary lesions in laparoscopic cholecystectomy as well as the readiness to convert early to the open procedure.

### 15.3.1 Critical View of Safety and Technical Points

A surgeon is always required to apply reliable surgical techniques to achieve division of the cystic duct and artery in either open or laparoscopic cholecystectomy. Misidentification of the extrahepatic bile duct anatomy during LC is the main cause of bile duct injury [5]. Meticulous dissection of the Calot's triangle and preparation of all relevant structures are the cornerstone of a safe laparoscopic cholecystectomy.

The CVS technique, which was first described by Strasberg et al. in 1995 [5], was introduced to reduce the risk of bile duct injury. A recent Society of American Gastrointestinal and Endoscopic Surgeons (SAGES) expert Delphi consensus deemed the CVS as being the most important factor for overall safety [15]. Nowadays, the CVS technique is the gold standard to perform a safe cholecystectomy with identification of the vital structures such as the cystic duct.

The reviewed literature suggests that judicious establishment of CVS could decrease bile duct injury rate, from an average 0.4% to nearly 0% [16].

To establish CVS, two windows need to be created during dissection of Calot's triangle: one window between the cystic artery, cystic duct, and gallbladder, and another one between the cystic artery, gallbladder, and liver. The CVS technique is aimed especially at mobilizing the gallbladder neck from the liver in the appropriate cystic plate to obtain a circumferential identification of the cystic duct and its transition into the gallbladder [5]. The guiding structure for dissection should be the wall of the gallbladder. Proper retraction of the fundus cephalad and of the infundibulum posteriorly and laterally is necessary, and tenting by excessive lateral pulling on the gallbladder should be avoided. Cephalad traction on the fundus compresses Calot's triangle, while lateral traction on Hartmann's pouch tents up the CBD, which may then be mistaken for the cystic duct, especially when that duct is very short. The cystic duct should be dissected in a retrograde fashion, starting at gallbladder proceeding with the identification of the cystic duct–gallbladder junction on both sides and the visualization of the cystic duct–common bile duct junction prior to clipping. Calot's triangle should be dissected from all fibrous and fatty tissues. At the end of the dissection, only the cystic duct and artery cystica should enter the gallbladder and the bottom of the liver bed should be visible. The CBD is not necessary to be exposed. Failure to achieve the CVS is an absolute indication for conversion or additional bile duct imaging [6]. The CVS should be described in the operative report.

Connor et al. and Wakabayashi et al. elegantly describe five key initial steps in performing safe laparoscopic cholecystectomy: (1) retract the gallbladder laterally to a 10 o'clock position relative to the principle plane of the liver (Cantlie's line); (2) confirm Hartmann's pouch is retracted up and towards segment IV; (3) identify Rouviere's sulcus which marks the level of the right posterior portal pedicle and is identifiable in >80% of the patients. An imaginary line drawn along the sulcus and carried across to the base of segment IV shows the level ventral to which dissection is "safe" and dorsal to which it is not; (4) dissect the posterior peritoneum of the hepatobiliary or hepatocystic triangle; and (5) confirm the critical view is obtained [12, 17].

Energy devices should be used cautiously in the of Calot's triangle with low cautery settings (<30 W), coagulation of small pieces of tissue at one time, and being sure that the coagulating surface is free of any adjacent tissue [6]. There are few data on the comparison between different energy devices in LC with respect to safety. Nevertheless, there was no significant difference between the use of ultrasonic and electrocautery energy with respect to postoperative bile leakage [15]. Sharp dissection increases the risk of bleeding, which presents added problems in controlling the bleeding when clips must be used blindly, or thermocoagulation is applied near the porta hepatis. Instruments should be kept in the field of vision at all times during dissection and instrument changes. Before ligation and division of any structure, its anatomical position should be defined clearly. Clips should be applied so that their tips are seen projecting beyond the duct, free of any extraneous material. In cases of thickened cystic duct, use of ligature loops or intracorporeal ligation is recommended instead of clips. Two loops should be applied on the side of the cystic duct to be retained. Applying extra clips is not the answer and may, in fact, lead to tenting injury [6].

### 15.3.2 Role of Intraoperative Cholangiography, Ultrasonography, and Fluorescence Imaging

Intraoperative cholangiography (IOC) is the most frequently applied technique for intraoperative assessment of the biliary anatomy. Although, for years, it has been speculated that IOC may decrease both the incidence and the severity of BDI, reports on the protective effect of routine IOC against BDI are conflicting, ranging from no benefit to a 40% risk reduction [18]. Van de Graaf et al. [19] in their systematic review compared routine versus selective use of IOC, and no clear conclusions could be drawn. IOC has been demonstrated to be a helpful tool in both prevention and intraoperative recognition of BDI. However, routinely application of this modality is not definitively recommended due to limited available supporting evidence. Accordingly, Ford et al. in their review made a similar conclusion: no robust evidence currently exists to either support or abandon the use of IOC in the prevention of BDI [20]. Additionally, IOC is prone to failure with a median reported success rate at 89%, involves radiation exposure, and requires additional equipment and manpower. An IOC has to be correctly performed and interpreted to assist the surgeon in identifying the CBD, and injuries may occur even if an IOC has been performed. A normal cholangiogram reveals flow of the contrast media into the duodenum, visualization of the proximal hepatic duct along with the right anterior and posterior sectoral ducts and left main duct, no filling defects within CBD, and presence of spiral valves within cystic duct. Advocates for omission of IOC also state that this technique might even be harmful to the patients due to the additional operative time and the risk of iatrogenic major BDI [19]. Moreover, the interpretation of an intraoperative cholangiography with potentially distorted anatomy clearly depends on the expertise of the surgeon. Thus, it may be argued that the absolute risk reduction associated with IOC does not warrant the added time and cost. Perhaps even more relevant than whether IOC in itself is useful is the question of whether it should be performed routinely or selectively.

Intraoperative ultrasonography (IOUS) is another imaging modality to identify and clarify the anatomy at Calot's triangle and hepatoduodenal ligament, less invasive than IOC. It has the potential to achieve high accuracy, with reports of completely visualizing the biliary tract in 92–100% of cases, with a failure rate that is lower than IOC [19, 21]. Although, the learning curve in the performance and interpretation of the ultrasonogram constitutes a major disadvantage [22, 23]. All evidence shows excellent results with laparoscopic IOUS in delineating the biliary anatomy. The advantages of laparoscopic IOUS over IOC are the shorter procedure time, its noninvasive nature, and lack of use of radiation. Furthermore, it may be performed prior to dissection in Calot's triangle and repeated in uncertain cases [24].

Indocyanine green (ICG) enhanced fluorescence near-infrared imaging is an emerging minimally invasive and easy modality for the visualization of the easier intraoperative recognition of the biliary anatomy. ICG can be injected into the human blood stream and becomes fluorescent once excited with specific light in the near-infrared spectrum, as it is exclusively by the liver after intravenous administration and has a very well-known pharmacokinetic and safety profile. ICG imaging allows repeatable and real-time exploration of the biliary system, something that is not possible with radiological IOC and provides relevant high detection rates of biliary tree structure, with specifically high detection rates of the cystic duct. Real-time simultaneous imaging of the bile ducts and the arterial anatomy (i.e., hepatic and cystic arteries) also can be obtained. Neither radiological support nor additional intervention such as opening the cystic or CBD is required, making it an easy, real-time, and flexible technique to use during surgery. However, the routine use of ICG fluorescence laparoscopy has not gained wide clinical acceptance yet due to a lack of high-quality clinical data. Furthermore, increased costs are involved in terms of the light source, camera, and fluorescent dye [25].

## 15.4 Classification of Bile Duct Injuries (BDI)

Several classification systems, such as Bismuth's classification, Hanover classification, Neuhaus classification, Siewert classification, Stewart-Way classification, and Strasberg classification, have been used to stratify bile duct injuries [5, 26–30]. Although the abovementioned systems are useful for standardization of outcome reporting and management decision-making, most of them fail to take into consideration significant prognostic factors, such as the mode of presentation, associated vascular injuries—particularly injuries to the right hepatic artery—, any longitudinal strictures of the common bile duct due to failed repair attempts, the presence of concomitant sepsis or secondary biliary cirrhosis, or segmental liver atrophy [31].

Classification of bile duct injuries is of paramount importance before planning any intervention because the type of treatment and optimal timing of treatment vary significant among the various types of BDI [32]. Relaparotomy should never be undertaken before adequate classification. Many injuries can be treated endoscopically with or without percutaneous drainage of any collections (i.e., bilomas). It is extremely important to identify the exact location of a BDI in order to select the optimal strategy for their management [32, 33].

Despite the presence of so many classification systems, the Bismuth and Strasberg systems remain the most popular and are used widely with the former being the first established in 1982 [27].

### 15.4.1 Bismuth Classification

Bismuth proposed a classification system of post-cholecystectomy benign biliary strictures (Fig. 15.1, Table 15.2) which was based on the lowest level at which healthy biliary mucosa is available for anastomosis, measured from the confluence of the right and left hepatic ducts [27]. It reveals a good correlation with the final outcome after attempted repair. Bismuth classification intended to help the surgeon to choose the appropriate technique for the repair and, although, it was established for biliary strictures, it is commonly implemented to acute BDI. This classification included five types (I to V) of bile duct injuries according to the level of the injury, the distance from the biliary bifurcation, the involvement of the bifurcation, or an anomalous right sectoral duct [34].

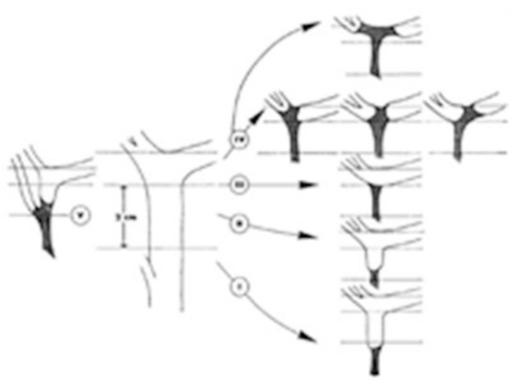


**Fig. 15.1** Bismuth classification. (From [34], with permission)

**Table 15.2** Bismuth classification

| Type | Injury type |
|---|---|
| I | Low CHD stricture, with a length of the CBD stump of >2 cm |
| II | Proximal CHD stricture with a length of the CBD stump <2 cm |
| III | Hilar stricture, no residual CBD, but the hepatic ducts' confluence is preserved |
| IV | Hilar stricture, with involvement of the confluence and loss of communication between right and left hepatic ducts |
| V | Involvement of an aberrant right sectorial hepatic duct alone or with concomitant stricture of the CHD or CBD |

Type I is associated with low common hepatic duct strictures, with a common hepatic bile duct stump longer than 2 cm, and can be repaired without opening the left hepatic duct and without lowering the hilar plate. Type II refers to proximal strictures, with a stump shorter than 2 cm, and requires opening of the left hepatic duct for a satisfactory anastomosis. Lowering the hilar plate is not always necessary, although it may improve the exposure. Type III lesions in the hilum, in which only the ceiling of the biliary confluence is intact, require lowering the hilar plate and anastomosis on the left ductal system. There is no need to open the right duct if the communication between the ducts is wide. With type IV lesions, the biliary confluence is interrupted and requires either reconstruction or two or more anastomoses, after lowering the hilar plate. Type V lesions are strictures of the hepatic duct (type I, II, or III) associated with a stricture on a separate aberrant right sectorial hepatic duct alone and that branch must be included in the repair [27, 34].

Although, this classification is applicable while evaluating long-term complications following bile duct injuries, it does not include the wide spectrum of all possible biliary injuries.

Sikora et al. [35] proposed that progression of fibrosis results in an intermediate stage between type III and type IV—according to Bismuth—strictures, where the floor of the confluence of the right and left hepatic ducts is scarred, although complete hilar isolation has not occurred. Consequently, hilar benign biliary strictures need to be subclassified, based on whether the floor of the confluence is healthy or scarred, as assessed by cholangiography or intraoperatively, because it influences the degree of operative difficulty and morbidity. Thus, patients with type III—according to Bismuth classification—strictures are subclassified into type IIIA hilar strictures, where the floor of the confluence was healthy and type IIIB hilar strictures, where the scarring involved the floor of the confluence. It is proposed that type IIIB strictures should be subclassified along with type IV strictures.

### 15.4.2 Strasberg Classification

Strasberg et al. [5, 36] reviewed the patterns of biliary injury and proposed a simplified, holistic classification based on the location of the injury in the biliary tract, combining not only the injuries proposed by Bismuth but also the early injuries. Although, this classification is very useful in determining the prognosis of an attempted repair, it does not take into consideration any additional vascular injuries. According to this system, there are five types (Fig. 15.2, Table 15.3) of common BDI (A–E).

Type A injuries occur due to leakage from the cystic duct stump or minor accessory radicals draining directly into the gallbladder (ducts of Luschka) and present as a biliary leakage and/or subhepatic biloma. Type B injuries are defined as ligation and division of an anomalous segmental duct—typically the duct draining segment VI—or right posterior sectoral duct (draining both segments VI and VII). This injury is often facilitated by the associated anomaly where the cystic duct drains into the right posterior duct. Type B injuries are usually subclinical or may have a delayed onset with abdominal pain or cholangitis involving the occluded liver segment. The occluded liver parenchyma will atrophy over time. Type C injuries occur in the same anatomic setting as type B injuries, though the proximal ductal segment is just divided and not occluded. Consequently, it leaks freely into the peritoneal cavity. This type of injury is often misdiagnosed, as ERCP typically misses the leaking segment because it is not opacified via the main biliary tree. Cholangiography should be carefully inspected to make sure all liver segments are visualized. In cases where the right posterior segments are not depicted, PTC may be not only diagnostic but will also allow leakage control. In type D injuries, a lateral injury—without major tissue loss—to the main bile duct occurs. This type of injury results either in an early leakage or

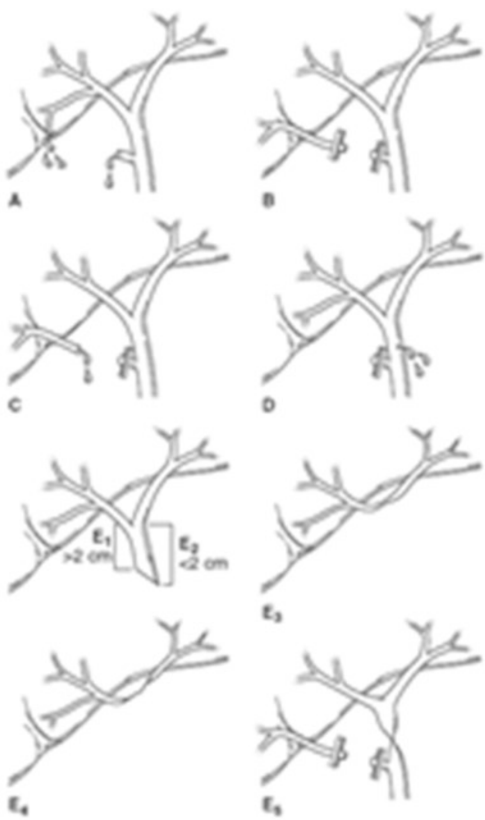



**Fig. 15.2** Strasberg classification [5, 36]

**Table 15.3** Strasberg classification

| Type | Injury type |
|---|---|
| A | Injury of small bile ducts in communication with the main biliary system, with leakage from cystic duct or from small ducts in the liver bed |
| B | Occlusion of an aberrant hepatic duct (almost invariably the right posterior sectoral duct) |
| C | Sectioning without ligation of an aberrant right hepatic duct |
| D | Lateral injury of the CBD |
| E1 | CBD injury at a distance>2 cm from the hepatic duct confluence |
| E2 | CBD injury at a distance<2 cm from the hepatic duct confluence |
| E3 | Hilar injury with preservation of the confluence of the hepatic ducts |
| E4 | Hilar injury with involvement of the confluence and loss of communication between the right and left hepatic ducts |
| E5 | Injury to an aberrant right sector hepatic duct or associated with a concomitant injury to the CBD |

in a delayed stricture and may be diagnosed accurately by ERCP, which can also provide a definitive treatment. Type E injuries are defined by complete disruption of the main bile duct due to transection, excision, and/or ligation of the extrahepatic biliary tree. Injuries that include a free biliary leakage will prevent early bile peritonitis and sepsis. Injuries with occlusion of the proximal hepatic drainage may present in a delayed fashion with jaundice and/or cholangitis. Type E injuries are further stratified to five subtypes (E1 to E5), according to Bismuth's classification system. E1 and E2 injuries result from a transected CBD or a stricture more or less than 2 cm from the biliary bifurcation, respectively. E3 injuries refer to a stricture of the biliary bifurcation with right and left hepatic ducts in communication. In type E4, the stricture of the biliary bifurcation results in separation of right and left hepatic ducts, whereas in type E5 a stricture of the main bile duct is associated with a transected right posterior sectoral duct. The majority of type E injuries will require PTC to definitively reveal the anatomic details of the injury and to establish stable biliary drainage.

Neither the Strasberg nor the Bismuth classification clearly describes one of the most serious injuries, namely that which presents as a biliary leak with separation of the right and left ducts resulting from excision of the extrahepatic biliary tree. For that, Connor et al. [31] proposed a sixth subdivision in type E injuries (E6), which is associated with complete excision of the extrahepatic ducts involving the confluence of the left and right hepatic ducts.

### 15.4.3 Siewert Classification

Siewert et al. [37] proposed four different types of BDI (Table 15.4). The most severe case is the lesion with a structural defect of the CBD or CHD with (IVa) or without (IVb) concomitant vascular injury. Tangential lesions without structural loss of the duct should be denominated as type III (stratified as IIIa and IIIB, according to the presence or not of additional vascular injury, respectively). Type II comprehends late strictures without obvious intraoperative trauma to the duct. Type I includes immediate biliary fistulae of usually good prognosis.

**Table 15.4** Siewert classification

| Type | Injury type |
|---|---|
| I | Immediate biliary fistulae |
| II | Late strictures without obvious intraoperative trauma to the duct |
| III<br>IIIa<br>IIIb | Tangential lesions without structural loss of the duct<br>With additional vascular injury<br>Without additional vascular injury |
| IV<br>Iva<br>IVb | Lesion with a structural defect of the CBD or CHD<br>With additional vascular injury<br>Without additional vascular injury |

**Table 15.5** Mattox classification

| Type | Injury type |
|---|---|
| I | Contusion of the gallbladder or portal triad |
| II | Partial gallbladder avulsion from liver bed; cystic duct intact<br>Laceration or perforation of the gallbladder |
| III | Complete gallbladder avulsion from liver bed<br>Cystic duct laceration/transection |
| IV | Partial or complete right hepatic duct laceration<br>Partial or complete left hepatic duct laceration<br>Partial common hepatic duct laceration (≤ 50%)<br>Partial common bile duct laceration (≤ 50%) |
| V | > 50% transection of common hepatic duct<br>> 50% transection of common bile duct<br>Combined right and left hepatic duct injuries<br>Intraduodenal or intrapancreatic bile duct injuries |

### 15.4.4 Mattox Classification

The Mattox classification (Table 15.5) of BDI takes into consideration a variety of injure patterns such as contusion, laceration, perforation, and transection of the biliary tree [38, 39].

### 15.4.5 McMahon Classification

McMahon et al. suggested that the type of injury may be subdivided into bile duct laceration, bile duct transection or excision, and bile duct stricture [40]. The level of stricture may be further graded according to the Bismuth's classification. Based on this classification, lacerations under 25% of the bile duct diameter or cystic–common bile duct junction ("buttonhole tear") were classified as minor ductal injury, whereas transection of CBD or CHD, or lacerations over 25% of bile duct diameter and postoperative bile duct stricture were classified as major injury [40]. Minor injury can usually be managed by simple suture repair and/or insertion of a T-tube, and major injury usually requires hepaticojejunostomy.

### 15.4.6 Amsterdam Academic Medical Center's Classification

Bergman et al. [41] from the "Amsterdam Academic Medical Center" identified four types of BDI (A–D). Type A is a leakage from the cystic duct or an aberrant or from peripheral hepatic radicles. Type B represents major bile duct leakage with or without concomitant biliary strictures, whereas type C corresponds to bile duct strictures without bile leakage. Type D refers to complete transection of the bile duct with or without excision of some portion of the biliary tree. The site of the ductal lesion was determined by its most proximal border (Table 15.6). Majority of type A and most type B lesions are amenable to stenting during ERCP, whereas majority of type C and all type D lesions require surgical intervention.

### 15.4.7 Neuhaus Classification

Neuhaus classification (Fig. 15.3) encompasses minor leaks from the gallbladder fossa or the cystic duct (type A) and major BDI including: occlusion of the CBD, CHD, right or left hepatic ducts by clips, either incomplete or complete (types B1 and B2, respectively), lateral lesions of the CBD, either small (<5 mm) or extended (>5 mm) (types C1 and C2, respectively), complete transections of the CBD or CHD, either without or with structural defect (types D1 and D2, respectively), and late strictures with stenosis of the extrahepatic bile ducts (type E). The latter group of BDI (E) is further stratified into four types: E1 and E2 with short (<5 mm) or long (>5 mm) stenosis of the CBD, respectively, E3 when the stenosis affects the confluence of the hepatic ducts, and E4 when there is stenosis of the right hepatic or a segmental duct (Table 15.7) [26, 42].

**Table 15.6** Amsterdam Academic Medical Center's classification

| Type | Injury type |
|---|---|
| A | Cystic duct leaks or leakage from aberrant or peripheral hepatic radicles |
| B | Major bile duct leaks with or without concomitant biliary strictures |
| C | Bile duct strictures without bile leakage |
| D | Complete transection of the duct with or without excision of some portion of the biliary tree |

The advantage of the Neuhaus' classification may be the ability to discriminate different injury patterns and recurrent cholangitis in the long term. Treatment strategies may be tailored according to the anatomical type of injury. However, this classification does not account for any concomitant vascular injuries [42].

### 15.4.8 Csendes Classification

Csendes et al. [43] proposed another classification, consisted of four types (I–IV) which has the advantage of classifying the severity of the lesions and proposing the appropriate management (Table 15.8). This system describes the mechanism of injury in detail and hence is useful while applying preventive strategies. However, it does not account for vascular injuries.

Type I corresponds to a small tear of the hepatic duct or right hepatic branch caused by dissection with the hook or scissors during the dissection of Calot's triangle. Type II, which is a new type of injury which was seldom seen during open surgery, corresponds to lesions of the cysticocholedochal junction due to excessive traction, the use of a Dormia catheter, section of the cystic duct very close or at the junction with the CBD, or to a burning of the cysticocholedochal junction by electrocautery. Type III corresponds to a partial or complete section of the CBD whereas type

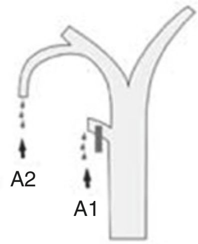
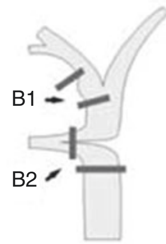
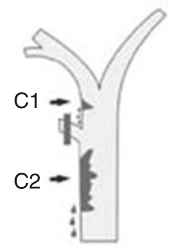
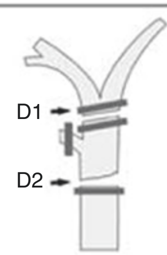
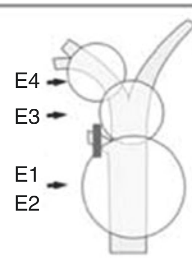
| | | |
|---|---|---|
| **Type A** | **Peripheral bile leak** (in communication with the CBD)<br><br>A1: Cystic duct leak<br>A2: Bile leak from the liver bed |   |
| **Type B** | **Occlusion of the CBD** (or right resp. left hepatic duct, i.e. Clip, ligation)<br><br>B1: Incomplete<br>B2: Complete |   |
| **Type C** | **Lateral injury of the CBD**<br><br>C1: Small lesion (< 5 mm)<br>C2: Extended lesion (> 5 mm) |   |
| **Type D** | **Transsection of the CBD**<br>(or right hepatic duct not in communication with the CBD)<br><br>D1: Without structural defect<br>D2: With structural defect |   |
| **Type E** | **Stenosis of the CBD**<br><br>E1: CBD with short stenosis (< 5 mm)<br>E2: CBD with long stenosis (> 5 mm)<br>E3: Confluence<br>E4: RIght hepatic duct/Segmental duct |   |

**Fig. 15.3** Neuhaus classification. (From [26], with permission)

**Table 15.7** Neuhaus classification

| Type | Injury type |
|---|---|
| A | Peripheral bile leak from the cystic duct (A1) or an accessory hepatic duct within gallbladder fossa (A2) |
| B | Occlusion of the CBD, or right/left hepatic duct (i.e clip, ligation): incomplete (B1) or complete (B2) |
| C | Lateral injury of CBD over a distance of up to 5 mm (small lesion, C1) or more than 5 mm (extended lesion, C2) |
| D | Transection of the CBD, or right hepatic duct not in communication with the CBD) without (D1) or with structural defect (D2) |
| E | Stenosis of the CBD |
| E1 | CBD with short stenosis (<5 mm) |
| E2 | CBD with long stenosis (>5 mm) |
| E3 | Confluence |
| E4 | Right hepatic duct or segmental duct |

**Table 15.8** Csendes classification

| Type | Injury type |
|---|---|
| I | A small tear of the hepatic duct or right hepatic branch caused by dissection with the hook or scissors during the dissection of Calot's triangle |
| II | Lesions of the cysticocholedochal junction due to excessive traction, the use of a Dormia catheter, section of the cystic duct very close or at the junction with the CBD, or to a burning of the cysticocholedochal junction by electrocautery |
| III | A partial or complete section of the CBD |
| IV | Resection of more than 10 mm of the CBD |

IV corresponds to resection of more than 10 mm of the CBD [43].

### 15.4.9 Stewart-Way Classification

Stewart-Way classification (Fig. 15.4) details the mechanisms and possible reasons for various classes of injuries and makes provision for combined biliovascular injuries, as well. This classification arose from the analysis of operative reports, providing the human mistakes and cognitive processes involved in the mechanisms of BDI. Stewart-Way classification groups BDI according to anatomic pattern and causation (Table 15.9) and encompasses four classes [44].

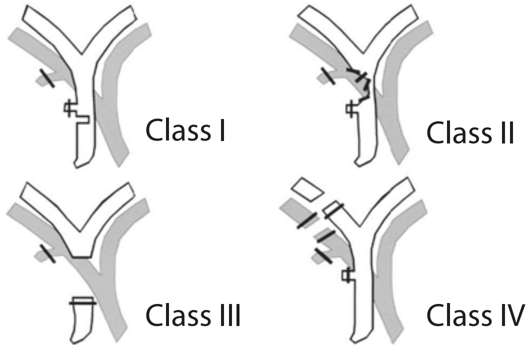



**Fig. 15.4** Stewart-Way classification. (From [44], with permission)

**Table 15.9** Stewart-Way classification

| Type | Injury type |
|---|---|
| I | Small incisions or incomplete intersections of the CBD<br>Cholangiogram incision in cystic duct extended into CBD |
| II | Lateral damage or stricture of the CBD caused by thermal injury or clips |
| III | Total transection or excision of the or CBD, CHD or the right or left hepatic ducts |
| IV | RHD mistaken for cystic duct, RHA mistaken for cystic artery RHD and RHA transected<br>Lateral damage to the RHD from cautery or clips placed on duct |

Class I injury occurs when CBD is mistaken for the cystic duct, but the error is recognized, usually by intraoperative cholangiography, before CBD is divided, or when the incision made in the cystic duct for the cholangiography is extended on to CBD. Class II injuries involve lateral damage to CHD from clips or cautery used too close to the duct. This often occurs in cases where visibility is limited due to inflammation or bleeding and results in stricture and/or fistula formation. Class III injury, the most common type, occurs when CBD is not recognized and mistaken for the cystic duct. The CBD, CHD, right or left hepatic ducts are transected, and a variable portion including the junction of the cystic and CBD is excised. Class IV injuries involve damage to the RHD or a right segmental hepatic duct, either because this structure is mistaken for the cystic duct or because it is injured during dissection or from cautery and/or clips placed on duct, often with injury of the right hepatic artery because it is mistaken for cystic artery (Fig. 15.4) [44].

### 15.4.10 Lau–CUHK (Chinese University of Hong Kong) Classification

This system stratifies the biliary injuries in an ascending order of severity from type 1 to 5 and emphasizes attention to operative detail to prevent these injuries. Type 1 injuries describe leaks from cystic duct stump or small ducts in liver bed. Type 2 refers to partial common hepatic or bile duct wall injuries without (2A) or with (2B) tissue loss, whereas type 3 to common bile or hepatic duct transection without (3A) or with (3B) tissue loss. Right or left hepatic duct or sectorial duct injuries without (4A) or with (4B) tissue loss constitute type 4 injuries. All bile duct injuries associated with vascular injuries encompass type 5 injuries (Table 15.10) [45].

### 15.4.11 Kapoor Classification

Kapoor [46] in a letter to the editor published a classification similar to ATOM [47] established by EAES, in that letters pertaining to the type of injury were used (nominal), rather than a categorical sequence. The proposed classification consisted of three types of injury (B,C,D) describing bile leakage, circumference involvement, and duct injury, respectively (Table 15.11). Every type has two subdivisions: By for open duct and Bn for ligated or clipped ducts, Cf when full circumference was involved due to either transection or excision and Cp when partial circumference was involved (clip, cautery, hole, excision), and Ds for significant duct (CBD,CHD, RHD, right sectoral, or segmental duct) injury and Di for insignificant duct (cystic duct, subsegmental duct, subvesical duct) injury. Vascular injury was included (the letter V is added when there is associated vascular injury), but there was no clear description of the level of the injury. However, the proposed classification is simple and easy to remember, reproduce, and interpret.

**Table 15.10** Lau - CUHK classification

| Type | Injury type |
|---|---|
| 1 | Leaks from cystic duct stump or small ducts in liver bed |
| 2 | Partial CBD/CHD wall injuries without (2A) or with (2B) tissue loss |
| 3 | CBD/CHD transection without (3A) or with (3B) tissue loss |
| 4 | Right or left hepatic duct or sectorial duct injuries without (4A) or with (4B) tissue loss |
| 5 | Bile duct injuries associated with vascular injuries |

**Table 15.11** Kapoor classification

| Type | Injury type |
|---|---|
| B | Bile leak<br>By-yes (open duct)<br>Bn-no(ligated/clipped duct) |
| C | Circumference involved<br>Cf-full circumference (transection or excision)<br>Cp-partial circumference (clip, cautery, hole, excision) |
| D | Duct injured<br>Ds-significant duct (CBD, CHD, RHD, right sectoral or segmental duct)<br>Di-insignificant duct (cystic duct, subsegmental duct, subvesical duct) |

### 15.4.12 Hannover Classification

Hannover classification delineated the injury patterns, including information regarding distal bile duct injuries and concomitant vascular injuries within the liver hilum. This classification provides discriminators for the localization of tangentially or completely transected bile ducts above or below the bifurcation of the hepatic duct, which is a major drawback of other classification systems. Furthermore, it is reproducible and ensures uniformity of reporting. In this classification, BDI were divided into five types from A to E [48].

According to Hannover classification, a type A injury describes a peripheral biliary leakage, either originating from the cystic duct (A1) or from the gallbladder bed (A2) with reconnection to the main bile duct system. This type of injury corresponds to type A and 1 injury according to Strasberg and Siewert classification, respectively, but Hannover classification further distinguishes a type A1 injury that leads to biliary leakage from the cystic duct and type A2 that is leakage from the liver bed of the gallbladder. Both Siewert and Strasberg classification systems do not clarify whether the leakage is from the cystic duct or the liver bed. Additionally, Bismuth and Stewart-Way systems do not delineate these types of lesions.

A type B injury describes either an incomplete (B1) or complete (B2) occlusion of the common or main bile duct or the right hepatic duct by clips or ligation without injury. Type C corresponds to a tangential injury of the CBD or CHD with further subdivisions: C1 for small punctiform lesions (<5 mm), C2 for extensive lesions (>5 mm) below the confluence, C3 for extensive lesions at the level of the hepatic bifurcation, and C4 for extensive lesions above the level of the confluence. Type D refers to a completely transected bile duct with further stratification as follows: D1 without defect below the hepatic bifurcation, D2 with defect below the hepatic bifurcation, D3 at hepatic duct confluence level (with or without defect), and D4 above the hepatic bifurcation level (with or without defect). Vascular injuries are included in type C and type D (Fig. 15.5). Type E injury is associated with strictures of the main bile duct at a late postoperative state at varying distances from the confluence and is classified into four subtypes: E1 when the stricture is short circular (<5 mm) at the main bile duct, E2 when the stricture is longitudinal

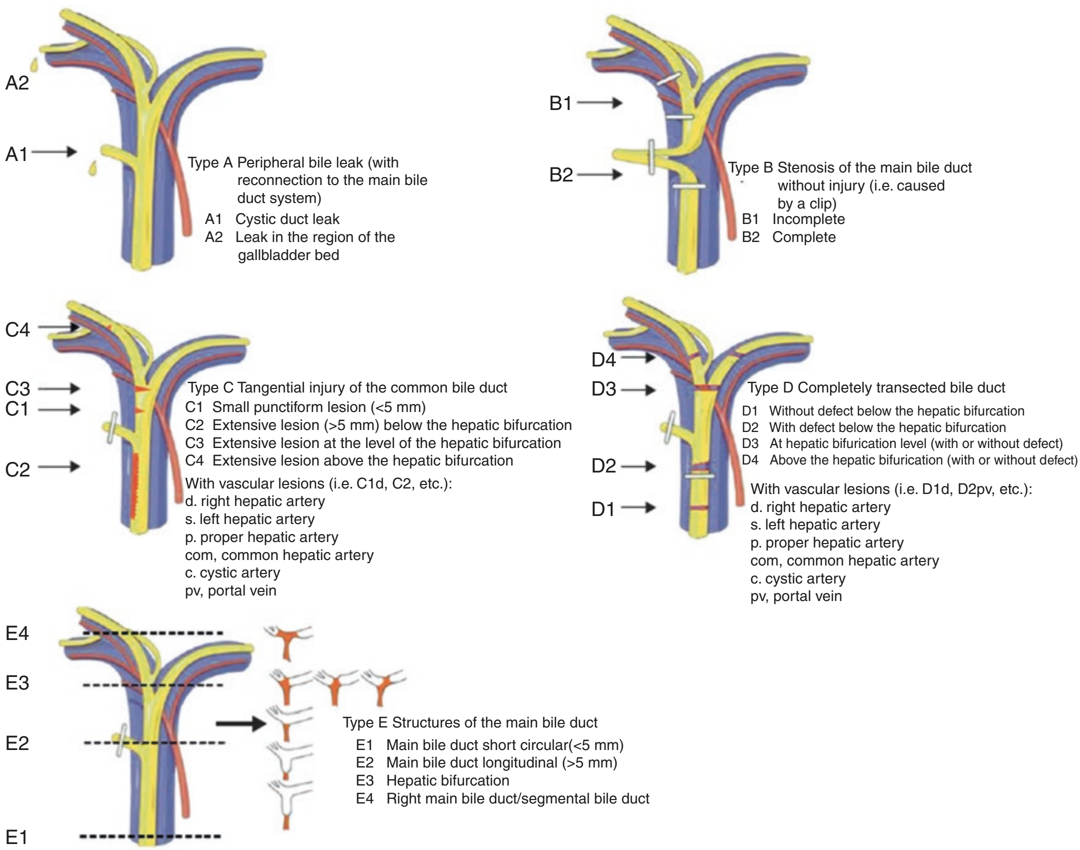



**Fig. 15.5** Hanover classification. (From [28], with permission)

**Table 15.12** Hannover classification

| Type | Injury type |
|---|---|
| A | Peripheal bile leakage (in communication with main biliary system) |
| A1 | Bile leakage from the cystic duct |
| A2 | Bile leakage from the gallbalder fossa |
| B | CHD or CBD stricture without damage (eg caused by a clip) |
| B1 | Incomplete |
| B2 | Complete |
| C | Lateral CHD or CBD injury |
| C1 | Small spot injury (<5 mm) |
| C2 | Large injury (>5 mm) below the hepatic ducts confluence |
| C3 | Large injury at the level of the hepatic ducts confluence |
| C4 | Large injury above the hepatic ducts confluence |
| D | Total transsection of CHD or CBD |
| D1 | Without ductal loss below the hepatic ducts confluence |
| D2 | With ductal loss below the hepatic ducts confluence |
| D3 | At the level of the hepatic ducts confluence |
| D4 | Above the hepatic ducts confluence (with or without ductal loss) |
| E | CHD or CBD stricture/stenosis |
| E1 | Short, circular (<5 mm) CBD stricture |
| E2 | Longitudinal CBD stricture (>5 mm) |
| E3 | Stricture at the level of the hepatic bifurcation |
| E4 | Stricture of the right hepatic duct or segmental duct |

(>5 mm) at the main bile duct, E3 when affects the hepatic confluence, and E4 when affects the right main bile duct or a segmental bile duct (Table 15.12) [48].

### 15.4.13 Cannon Classification

Cannon et al. [49] devised a simple, three-tier classification scheme with the primary goal of stratifying injuries based on the financial cost of definitive management. Grade I injuries consisted of leaks from the cystic duct stump, duct of Luschka, or accessory right hepatic ducts. Grade II injuries consisted of all other levels of biliary injury, including those to the common bile duct or intrahepatic bile ducts. Grade III includes all combined vascular and biliary injuries. However, this system does not provide the precise anatomic information afforded by current classification schemes, though its simplicity makes it applicable to routine clinical practice.

### 15.4.14 ATOM Classification

Several classifications have been proposed to stratify the type of injury and to standardize the treatment strategy [47]. For each classification, however, one or more relevant features of BDI necessary to thoroughly describe its complexity are lacking [50–52]. For this reason, the European Association for Endoscopic Surgery (EAES) proposed an all-inclusive BDI nominal classification system (ATOM), which includes the anatomy of damage and occurrence of vascular injury (A), the timing of detection (To), and the mechanism of damage (M) [47, 50–52] (Table 15.13).

The parameter "anatomic characteristics of the injury" includes the anatomic level on the biliary tree of the initial injury and concomitant vasculobiliary injury [47]. The biliary tree is divided into the main and nonmain biliary ducts. The main biliary duct (MBD in the EAES classification) (including the CBD, the CHD, and the right and left hepatic ducts) derived from the Bismuth, Strasberg, Neuhaus, Connor, McMahon, and Lau classifications [5, 6, 26, 31, 34, 40, 45]. The anatomic localization is as follows: type 1, low main BDI ≥2 cm distal to inferior border of superior hepatic confluence; type 2, middle main BDI <2 cm distal to inferior border of superior hepatic confluence; type 3, high main BDI involving the superior hepatic confluence but the left–right communication is preserved, usually on the roof; type 4, high main BDI involving the superior hepatic confluence but left–right communication is interrupted, including the E6 injury of Connor and Garden [31]; type 5, left or right hepatic duct injuries without injury to the superior confluence; and type 6, isolated segmental hepatic duct injury [53].

The nonmain biliary duct (NMBD in the EAES classification) includes the cystic aberrant and accessory (hepatic bed, subhepatic, or Luschka) ducts, corresponding to Strasberg types A and C, Neuhaus A, Lau 1, and Amsterdam type

**Table 15.13** EAES classification matrix for bile duct injuries

| Anatomical characteristics | | | | | | | Time of detection | | | Mechanism | |
|---|---|---|---|---|---|---|---|---|---|---|---|
| Anatomic level | Type and extent of injury | | | | | Vasculobiliary injury (yes = VBI+) and name of injured vessel (RHA, LHA, CHA, PV, MV); (no = VBI-) | Ei (de visu, bile leak, IOC) | Ep | L | Me | ED |
| | Occlusion | | Division | | | | | | | | |
| | C | P[a] | C | P[b] | LS[b] | | | | | | |
| MBD | | | | | | | | | | | |
| 1 | | | | | | | | | | | |
| 2 | | | | | | | | | | | |
| 3 | | | | | | | | | | | |
| 4 | | | | | | | | | | | |
| 5 | | | | | | | | | | | |
| 6 | | | | | | | | | | | |
| NMBD | | | | | | | | | | | |

For each injury, the surgeon fills in the following matrix: (1) single injury (yes/no); (2) multiple injuries (yes/no). Then one matrix is filled in for each injury, as appropriate. For example, an injury made by an energy-driven (ultrasonic) dissector involving the superior biliary confluence with interruption of the right and left hepatic ducts, detected (intraoperatively) during the operation by the presence of bile would be classed as MBD4 CVBI Ei, ED. The Connor Garden E6 injury is in fact a type 4 with LS: MBD 4 LS

*EAES* European Association for Endoscopic Surgery, *MBD* main biliary duct, *NMBD* nonmain biliary duct (Luschka duct, aberrant duct, accessory duct), *level 1* $\geq$ 2 cm from lower border of superior biliary confluent, *level 2* < 2 cm from lower border of superior biliary confluent, *level 3* involves the superior biliary confluent but communication right left is preserved, *level 4* involves superior biliary confluent but communication right left is interrupted, *level 5a* right or left hepatic duct, *level 5b* right sectorial duct but bile duct still in continuity, *C* complete, *P* partial, *LS* loss of substance, *Me* mechanical, *ED* energy driven, *VBI* vasculobiliary involvement, *RHA* right hepatic artery, *LHA* left hepatic artery, *CHA* common hepatic artery, *PV* portal vein, *MV* marginal vessels, *Ei* early intraoperative, *Ep* early postoperative, *L* late, *OC* intra-operative cholangiogram

[a]Indicate percentage of circumference, if known

[b]Indicate length, if known

A [5, 26, 33, 34, 42, 45]. The type as well as the circumferential and longitudinal extent of injury depends on whether the injured bile duct was initially occluded (O) (ligation, clip, sealed) or divided (D) and leaked. In both of these, the lowercase letter "c" is added to stand for complete interruption (ligation, clip, sealing, or division), while a partial interruption (ligation, clip, sealing, or division) is labeled "p," followed by the percentage of the circumference involved whenever this detail is known, whether there was a loss of substance between two divisions, irrespective of whether one or both of the extremities was occluded or divided (LS; the length in centimeters, whenever known, is indicated in parentheses). Concomitant vasculobiliary injury (VBI) is defined as an injury to both a bile duct and a nearby vessel [5]. Our definition also includes vascular injury that occurs alone in the index operation but results in injury, such as septic complications, stricture, or liver atrophy.

The parameter "time of detection" is classified as early (E), either intraoperative or late (L). The early detection group is further stratified according to the intraoperative (Ei) or immediate postoperative detection, whereas the former is usually discovered by the presence of bile in the operative field or at intraoperative cholangiography [27, 31, 45].

The parameter "mechanism of injury" may be classified as mechanical (Me) (e.g., scissors) or energy driven (ED) (e.g., cautery or ultrasonic) injury. The EAES classification label for BDI thus includes a series of acronyms: MBD for main bile duct (followed by a number 1–6, corresponding to the anatomic level on the main bile duct), NMBD for nonmain bile duct, followed by the relevant acronyms (Table 15.13): O or D, each with the suffix c or p (%), LS (cm), VBI (RHA, LHA, CHA, PV, marginal vessel [MV]), Ei, Ep, or L, and Me or ED. If for some reason a parameter is unknown, the suffix "?" is added [47].

Although, the classification may appear complex, ATOM is the only classification that allows true comparisons with the others because it is all-inclusive, and there are no missing details (as in the case with others) [50–52]. It includes objective data and not subjective terms, such as major, minor, peripheral, central, significant, and insignificant. It allows comparisons of mechanisms and timing of BDI between the other classifications. Last but not least, it emphasizes the underlying mechanism that led to the injury, the most relevant aspect for didactic purposes aiming at prevention [50–53].

## 15.5 Conclusions

Preventive strategies and safe surgery are of utmost importance to minimize BDI during laparoscopic cholecystectomy. Although many methods used in the prevention of BDI have demonstrated promising results, there is no consensus regarding a systematic reporting system of BDI. Currently, CVS seems to be the cornerstone for a safe laparoscopic cholecystectomy. In difficult cases, a sufficient attention to alternative techniques should be apprehended. In such cases, intraoperative imaging may delineate the biliary anatomy.

In order to define the type of BDI, several classifications have been proposed, but none is universally accepted. The heterogeneity of these classifications reduces their clinical utility and each of them has limitations. Although, they are useful for standardization of outcome and predictive quality, important short-term prognostic factors, including recognition of injury, mode of presentation, previously attempted repairs, presence of concomitant sepsis, and stability of the patient, are not accounted in most of the classification systems, and the documentation of an associated vascular injury has been described only recently. Furthermore, their complexity makes their routine incorporation into clinical use difficult. Among them, Bismuth's and Strasberg's classifications are most commonly used by clinicians. Recently, EAES devised an all-inclusive, semantics-based, nominal classification "ATOM" (Anatomic, Time Of detection, Mechanism) combining all existing classification items, which enables combination of all information on BDI, irrespective of the original classification used.

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# 16 Iatrogenic Lesions of the Biliary Tree: The Role of a Multidisciplinary Approach

Sergio Calamia, Duilio Pagano, and Salvatore Gruttadauria

## 16.1 Background

The gold standard for symptomatic cholelithiasis is laparoscopic cholecystectomy (LC), one of the most widely performed abdominal surgical procedures worldwide. Unfortunately, when compared to open cholecystectomy, it is correlated to a relevant incidence of surgical bile duct injury (SBDI), representing 0.1% to 0.2% in the era of open cholecystectomy and 0.4% to 0.7% in the era of minimally invasive cholecystectomy [1, 2].

The indicators and factors in question and that can contribute to the increase of SBDIs are: [3, 4].

- Incorrect recognition of the common biliary duct anatomy;
- Presence of a right or aberrant bile duct such as a cystic duct followed by its excision, division or occlusion;
- Excessive gallbladder traction and consequent retraction of common biliary duct;
- Devascularization or thermal damage to the main biliary tree;
- The operating surgeon's experience and learning curve effects;
- Local operating factors, including inflammation, the presence of a pathological accumulation of adipose tissue, the onset of hemorrhage during the surgical dissection, and too deep a dissection of the gallbladder bed; and
- Equipment problems such as laser use or clip failure.

These elements can lead to complex clinical conditions in which SBDI following cholecystectomy can easily represent an iatrogenic catastrophe, associated with worsening clinical outcomes, and quality of life.

## 16.2 Surgical Decision-Making

To define the optimal treatment, it is crucial when the extent of the main SBDI lesion, the patient's clinical status, and a rapid availability of a tertiary hepatobiliary referral center are recognized.

The localized inflammatory state is one of the main determinants of the prognosis of definitive repair surgery. Ideally, the inflammatory changes

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can alter the complexity of surgical repair and/or reconstruction procedures. Consequently, an immediately intraoperative repair by an experienced hepatobiliary surgeon is recommended.

When an SBDI is suspected, the surgeon must evaluate the cholangiographic biliary anatomy in order to avoid further dissections. This is essential, otherwise further biliary duct devascularization or lesion may occur [5, 6]. In several cases, an open procedure is necessary to obtain a proper identification of the biliary anatomy.

In cases of technically complex biliary lesions to be treated, it is useful to place several laparoscopic drainages to avoid the formation of abdominal collections and to place a percutaneous trans-hepatic drainage of the biliary tree, so as to transform the SBDI into a monitored biliary leakage. At that point, it is appropriate to refer the patient to a hepatobiliary surgical referral center [7, 8]. A literature review shows that in cases in which the lesions are repaired by an expert surgeon, complications are significantly reduced (94% success for an experienced hepatobiliary surgeon versus 17% for an inexperienced surgeon), hospital stay (222 days vs. 78 days), and mortality decreased (0% vs 1.6%) [9].

The aim of the intervention is to restore the integrity of the damaged biliary tract in order to prevent the onset of short- or long-term complications, such as biliary leakage or stenosis, chronic cholangitis, abdominal abscesses, or secondary cirrhosis. The best time to repair the damaged biliary tract is during the first surgery but, unfortunately, in only 25%–32.4% of cases is the lesion recognized on that occasion. Much more often, an SBDI will occur in the first postoperative days after LC.

The clinical symptoms are fever, mild hyperbilirubinemia, and pain related to biloma or biliary peritonitis. Usually, bile is seen exiting externally from a drain or surgical incision. When lesions involving common bile or hepatic duct occlusion without intraperitoneal bile loss, jaundice with or without abdominal pain is the principal symptom. Sometimes, patients can experience recurrent cholangitis or end-stage liver disease (cirrhosis) from a remote SBDI later, typically months after surgery.

Some patients can experience sepsis from intra-abdominal fluid collections or recurrent cholangitis. It is first mandatory to check for sepsis, eventually drain the abdominal collections, and define the type and description of SBDI and other associated damages. An urgent laparotomy is justified only in cases of severe biliary peritonitis not responsive to percutaneous drainage or other conservative maneuvers. In a clinical picture of peritonitis, biliary tree repair is statistically disadvantageous. It is therefore appropriate, if possible, to postpone the surgery 4–6 weeks, when the inflammation and local infection are better controlled.

## 16.3 Surgical Bile Duct Injury Classification

SBDIs are classified according to anatomic picture and clinical entity of biliary transection. Here we present the classification proposed by Dr. Stewart et al. [10].

### 16.3.1 Stewart-Way Class I Injuries

The lesion is localized to the duct that joins the gallbladder to the common hepatic duct (cystic duct) and/or to a peripheral duct on the hepatic parenchymal bed. A leakage of the cystic stump occurs because of a defective clip application, clip slipping, tissue necrosis close to the clip application for the diathermic injury, or an obstructive common bile duct (CBD) stone. Generally, the damage is recognized during surgery and can therefore be quickly repaired using an absorbable fine monofilament suture if necessary. There is no indication for placing a catheter with a T-tube, as insertion of the tube itself would result in an extension of the lesion and would increase the risk of stenosis [11]. If the lesion is detected after surgery, the gold standard is an endoscopic treatment through sphincterotomy, possibly by inserting a nasal tube or an internal biliary stent to reduce the gradient of the intraductal pressure maintained by the Oddi sphincter and remove the biliary flow from the damaged spot. The success rates of endoscopic sphincterotomy are very high (near 100%) [12].

To promote faster healing, most authors recommend the insertion of biliary stents, as opposed to sphincterotomy, for reducing the intraductal biliary tree pressure and for a prompt leakage covering. Not performing sphincterotomy also means avoiding related complications. Placing a nasal tube in a timely way obviates the need for several endoscopic retrograde cholangiopancreatographies (ERCPs). Otherwise, it might lead to several disadvantages: accidental movement of the tube, worsening of patient comfort, and increase in hospital length of stay.

ERCP has limits in cases of aberrant or sectioned bile ducts, or in cases in which the ducts do not communicate with the CHD (for example, aberrant right hepatic duct), or in cases of complete transection of the bile duct. In these cases, percutaneous trans-hepatic cholangiography (PTHC or PTC) is necessary in order to visualize the damaged duct and to define the lesion and the necessary biliary drainage.

### 16.3.2 Stewart-Way Class II Injuries

The lesion is a lateral damage of the CHD, resulting in stenosis and/or leakage. The treatment of biliary loss requires a multidisciplinary approach with endoscopy and drainage with radiological guidance as the first therapeutic approach. Stewart-Way Class II lesions with stenosis can be treated with multiple plastic stents and self-expanding covered metal or biodegradable stents, related to the SBDI severity [13]. Surgery is clearly reserved for cases in which conservative treatment fails.

### 16.3.3 Stewart-Way Class III Injuries

This lesion type includes a complete CBD/CHD transection. The treatment is mostly operational, though in some specific cases a minimally invasive extra-anatomic reconstruction (radiological or/and endoscopic therapies) can provide a safe and definitive option.

Some studies have proposed a combined endoscopic and radiological technique for the treatment of complete transection of the main bile duct, thus avoiding having to perform a highly risky intervention [14].

In the event that surgery is required, an end-to-end ductal repair can be performed without tension. End-to-end biliary duct repair of laparoscopic SBDI is burdened by a high rate of biliary stenosis. On the other hand, hepaticojejunostomy with a Roux-en-Y limb is certainly easier and allows you to perform an anastomosis without tension. For biliary lesion of diathermy, anastomosis has to be performed proximally to the biliary tree confluence to reduce the rate of sclerotic changes related to diathermic jeopardizing of the collateral vascular supply of CBD/CHD.

### 16.3.4 Stewart-Way Class IV Lesions

This fourth type of biliary lesion is localized in the right/left hepatic duct or in the sectoral duct and are often nonoperatively managed with a drainage and/or a stenting via ERCP or PTC.

A bile duct transection might require a reconstruction of the RHD with a hepaticojejunostomy and Roux-en-Y limb.

## 16.4 Surgical Treatment and ISMETT Clinical Experience

To define a correct reparative surgery, there are some basic rules to follow. First, the identification of size of the damaged biliary duct and the related extension of the local acute inflammatory and sclerotic changes. The detection timing should not lead the surgical team to delay the operative procedures and is a crucial factor: a specific assessment by a multidisciplinary team of surgeons, anesthesiologists, skilled nurses, interventional radiologists, endoscopic gastroenterologists, and physical and respiratory therapists, specifically trained for the care of patients with hepatobiliary disease. The aim of these meetings is to review individual clinical cases and must estimate the life expectancy and, above all, the social and family living conditions. An aggressive treatment plan must be weighed against the patients' needs and family organization. Only in the case of a partial or a complete CBD transection, a rapid direct end-to-end suture can be performed if the distal bile duct is free and without intensive inflammation. To avoid tension, a Kehr T-tube can protect the suture [15, 16]. Alternatively, an internal Y biliary drainage is useful to split the anastomosis by inserting the two branches into the RHD and LHD and leading its main branch in the duodenum. These tubes should be removed with an endoscopic procedure after healing of the biliary anastomosis. When a direct suture is not suitable, or only in cases of severe biliary sclerotic inflammatory changes, a hepaticojejunostomy with a Roux-en-Y limb is recommended [17–19].

If dense adhesions with infected and friable tissues can alter the anatomy of the hepatic hilum, and a hepaticojejunostomy with a Roux-en-Y limb cannot be safely performed, it has been suggested to combine endoscopic biliary stenting as a bridge treatment, followed by a biliary repair with hedged patches to reduce bile loss and sepsis. Recently, treatment of an SBDI with a hepaticojejunostomy with a Roux-en-Y limb reconstruction even with minimally invasive surgical approaches has been proposed. The robotic approach has demonstrated good results and a similar safety and feasibility to the laparoscopic technique in achieving the primary hepatic patency of the hepaticojejunostomy for bile duct repair [20–22].

SBDIs are often associated with vascular lesions [21]. The incidence of post-cholecystectomy vascular lesions is 16.7%–47%, typically with the interruption of the right hepatic artery due to the close CHD anatomical relationships. Unlike biliary lesions, it usually does not lead to significant early complications. Therefore, without a proper computed tomographic evaluation, it can likely remain unnoticed in most patients.

Generally, due to portal flow and arterial blood supply from collateral arteries, hepatic artery ligation can be tolerated without major clinical consequences [23]. During surgical SBDI repair, an associated lesion of arterial supply can lead to a more complex reconstruction, an increase in intraoperative bleeding, and biliary stenosis. Liver ischemia or end-stage liver disease due to biliary stenosis can cause partial liver atrophy/necrosis and may require a major hepatic resection or liver transplant. A rapid recognition of concomitant vascular lesions is necessary in order to propose surgical repair and major clinical sequelae [24].

Our case series of SBDIs and types of treatment performed are presented in Table 16.1. We have adopted a study protocol for SBDI patients. It involves the radiological study with triphasic computed tomography and magnetic resonance cholangiography to confirm the diagnosis of SBDI, classify it, and exclude any associated vascular lesions. In our experience, percutaneous catheter dilatation of trans-hepatic biliary drainage (PTBD) or ERCP is recommended first as a treatment for post-LC biliary stenosis and/or leaks for diagnostics and children. The surgical procedure is reserved for cases in which radiological or endoscopic procedures have proved ineffective or in cases of serious vascular damage. At ISMETT, 54 patients with SBDI have been transferred from other centers over the past 20 years. The majority of patients were surgically treated (26, 48%), while in 20 cases (37%) patients were treated with ERCP. In 8 of 54 cases (15%), percutaneous treatment was performed. Our experience further suggests that, in this light, a rapid tertiary referral hepatobiliary surgical treatment can reduce the role of surgery on the

**Table 16.1** Total number of patients admitted with a post-cholecystectomy iatrogenic lesion

| N | 54 |
|---|---|
| Period | No. (%) |
| 1999–2005 | 6 (11) |
| 2006–2010 | 7 (13) |
| 2011–2015 | 21 (39) |
| 2015–2020 | 20 (37) |
| Type of treatment | No. (%) |
| Surgical procedures | 26 (48) |
| Endoscopic procedures | 20 (37) |
| Percutaneous procedures | 8 (15) |

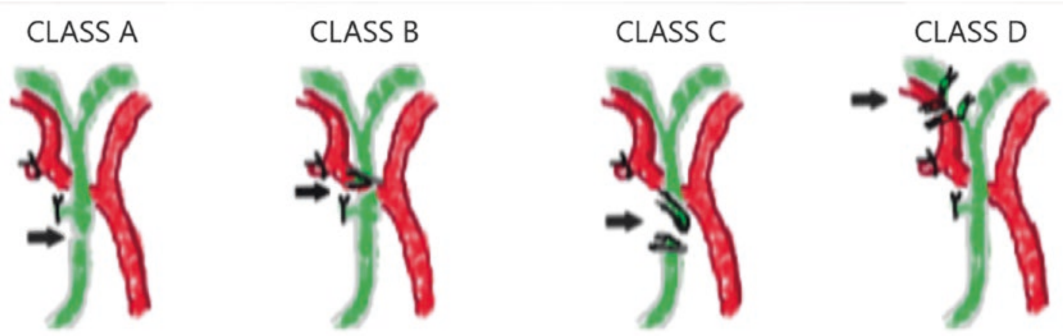


**Fig. 16.1** Stewart-Way classification of bile duct injuries

patient and allows extension of the minimally invasive indications for patients with a complex SBDI (Fig. 16.1).

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