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Routine and Innovation in Surgical Therapy of Gallstones

Peter Dubovan, Ramadan Aziri and Miroslav Tomáš

Abstract

This chapter discusses the anatomy of the gallbladder with the anatomical variations potentially impacting surgical therapy. It is dissertated upon the clinical indication for the surgical therapy with consecutive treatment. The discussion on the surgery focuses on the patient's safety and strategies for safe cholecystectomy with an optimal approach. Even though the efforts to minimise potential complications are made, the complication may arise, and therefore, the last part of this chapter discusses such cases with optimal clinical management.

Keywords: gallbladder anatomy, indication, surgical treatment, cholecystectomy, critical view of safety, complications, biliary injury

1. Introduction

The advancements in current knowledge of the human anatomy and diseases continuously led to innovation and improvements in surgical fields, with gallbladder surgery not being any different. Most of the advances were made in the last two centuries, lending the surgical pioneers perpetual reminiscence among colleagues. The names like Jean-Francois Calot, William S. Halsted, Carl Langenbuch, and others paved the way for successful gallbladder drainage and removal [1]. The introduction of open cholecystectomy led to the formation of new standards of care for the therapy of gallstones [1]. Moreover, the first video-laparoscopic gallbladder removal performed by French surgeon Philip Mouret meant the rapid spread of this new technique with majority replacement of the open surgery and changes to the state-of-the-art gallstone therapy making it in the process one of the most frequent surgeries currently performed worldwide [1, 2].

2. Anatomy of the gallbladder and the adjacent area

To perform a successful gallbladder surgery, the surgeon has to know the anatomy of this region and also be aware of potential anatomical variations resulting in a potentially more difficult surgery.

2.1 Biliary tract

Most of the time, the intrahepatic biliary ducts consecutively join forming anterior and posterior segment ducts, which drain into the right hepatic duct, and medial and lateral segment ducts draining into the left hepatic duct. The union of

the right and left hepatic ducts in the porta hepatis leads to the formation of the common hepatic duct (CHD) with its distal end formed by cystic duct junction and variation in the length from 1.0 to 7.5 cm depending on the junction site with the diameter of 0.4 cm [3].

In most people, the cystic duct joins the common hepatic duct at an angle of 40° from the right side and runs parallel to the CHD for a shorter or longer distance on average for 17 mm [3]. In some cases, the cystic duct may cross the CHD posteriorly or anteriorly and join the CHD from the left side [3].

Common bile duct (CBD)/ductus choledochus is formed by the union of the CHD and the cystic duct with its distal end at the papilla of Vater in the duodenum [3]. If the cystic duct enters the duodenum separately, the common bile duct is absent [3]. Standardly the length of CBD is diverse between 5 cm and 15 cm with an average diameter of 6 mm.

Gallbladder is a pouch 7–10 cm long able to contain 30–50 ml of bile and located on the visceral liver surface in the proximity of the liver segments IV and V [3]. Liver and gallbladder are separated by the Glisson capsule's connective tissue and anteriorly, the gallbladder is covered with the peritoneum completely enfolding the *fundus* [3]. Body of the gallbladder contacts the superior and descending part of the duodenum and the transverse colon [3]. Infundibulum is the posterior part of the gallbladder body between the neck and cystic artery entrance [3]. Dilated infundibulum with a lateral bulge is called the Hartman's pouch, formerly thought to be a variation, however later regarded as a constant feature [3]. Gallbladder neck is an S-shaped narrowing continually proceeding into the cystic duct (**Figure 1**) [3].

2.2 Vasculature of the gallbladder

The blood supply to the gallbladder is secured by the cystic artery, which commonly arises from the right hepatic artery (RHA) and runs towards the gallbladder

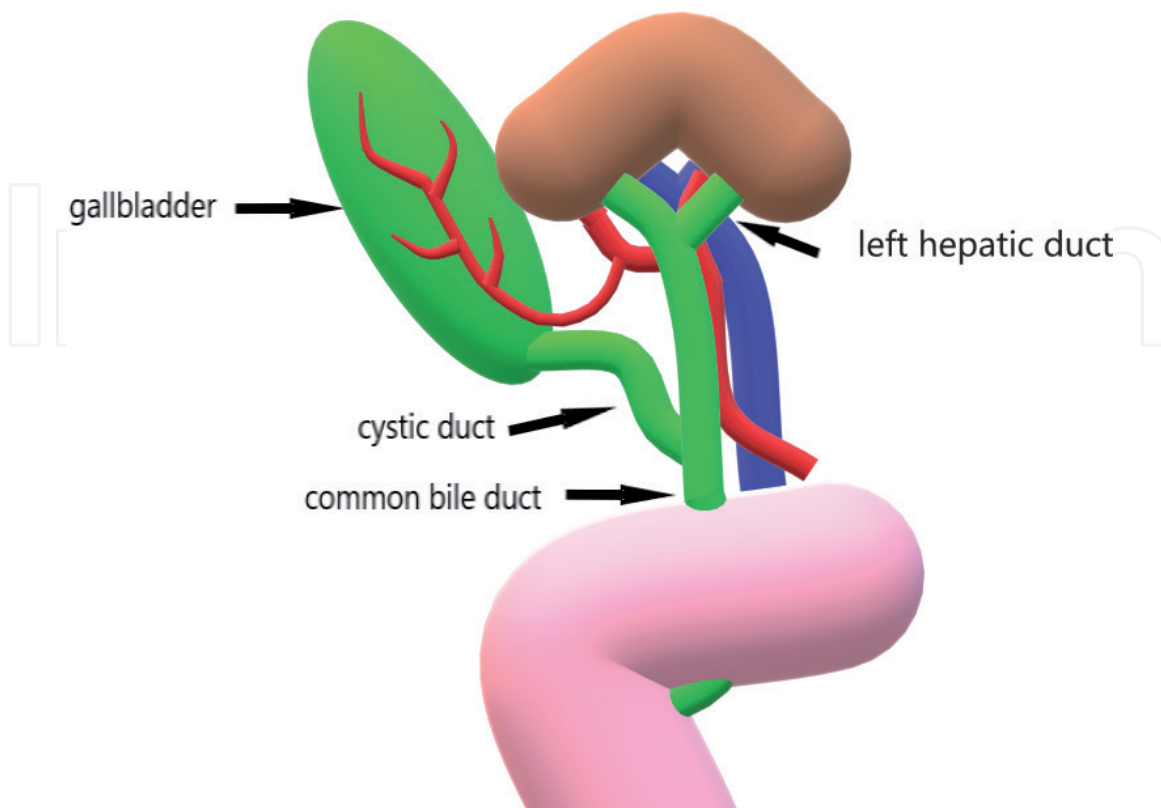


Figure 1.
Schematic image of the extrahepatic biliary tree with hepatic artery and portal vein.

just right to the common hepatic duct through the hepatocystic triangle [3]. Venous drainage is secured by a number of small veins passing through the gallbladder bed to the liver from the hepatic site, and from the peritoneal site, small veins drain into the liver through the ascending veins of the common bile duct [3]. The lymphatic drainage is secured by the collecting trunks draining into the cystic node localised in the angle between the cystic and common hepatic ducts and into the hiatal node localised on the anterior border of the epiploic foramen [3].

2.3 Hepatocystic triangle/triangle of Calot

The hepatocystic triangle is formed on the right side by the proximal part of the gallbladder and the cystic duct, on the left side by the common hepatic duct with the superior part being formed by the liver margin (**Figure 2**) [3]. Originally, the superior border of the Calot's triangle was the cystic artery; however, this area enlarged throughout the years [3]. Several structures run in the hepatocystic triangle, which have to be identified prior to any definitive surgical intervention. We have to visualise the right hepatic artery, cystic artery, common hepatic duct, and potential variations either in vascular or in biliary system [3].

2.3.1 Biliary variations in hepatocystic triangle important for gallbladder surgery

The right and left hepatic duct mostly joins at the level of the porta hepatis; however, in some individuals, this connection may be more distal eventually resulting in the absence of the common hepatic duct and potentially endangering the right hepatic duct during the surgical intervention (**Figure 3A**) [3]. Accessory hepatic duct can drain into the cystic duct or it may be mistaken for the cystic duct, and therefore, the surgeon has to be careful where to ligate the cystic duct during the surgery to preserve its function (**Figure 3C and D**) [3]. A similar problem arises with the duplication of the cystic duct, which may drain into the right hepatic duct, and therefore in the case of the omission of such anomaly leads to a biliary leak (**Figure 3E**) [3].

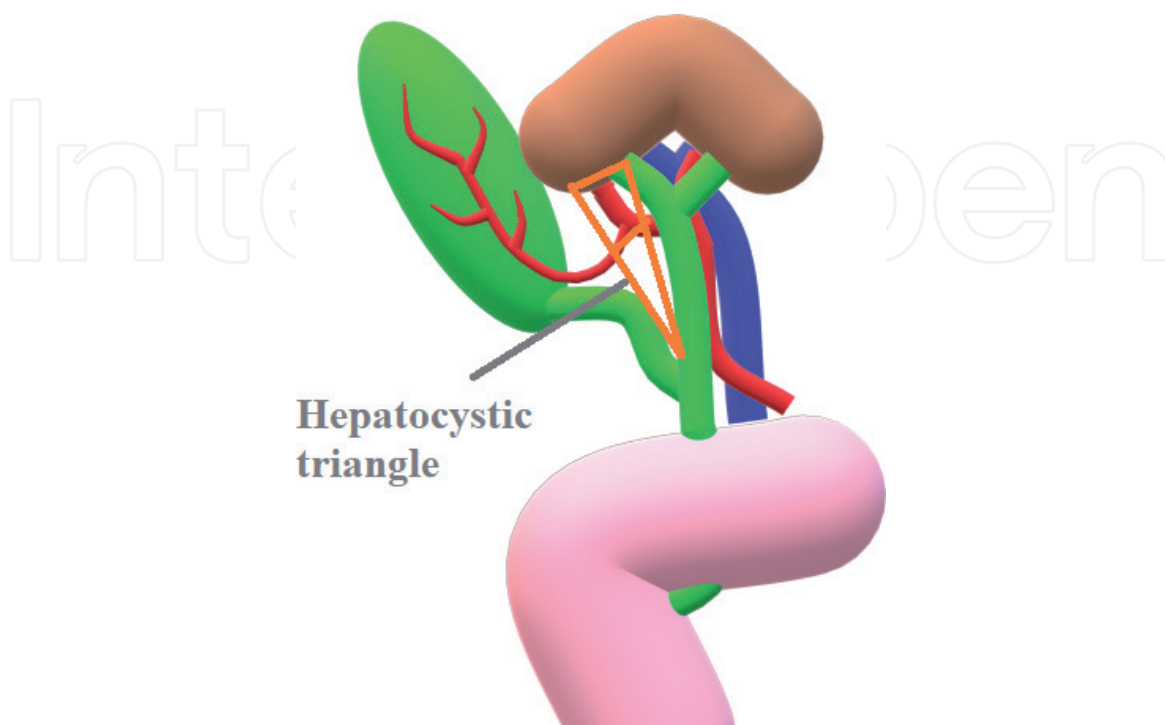


Figure 2.
Schematic image of the extrahepatic biliary tree with identified hepatocystic triangle.

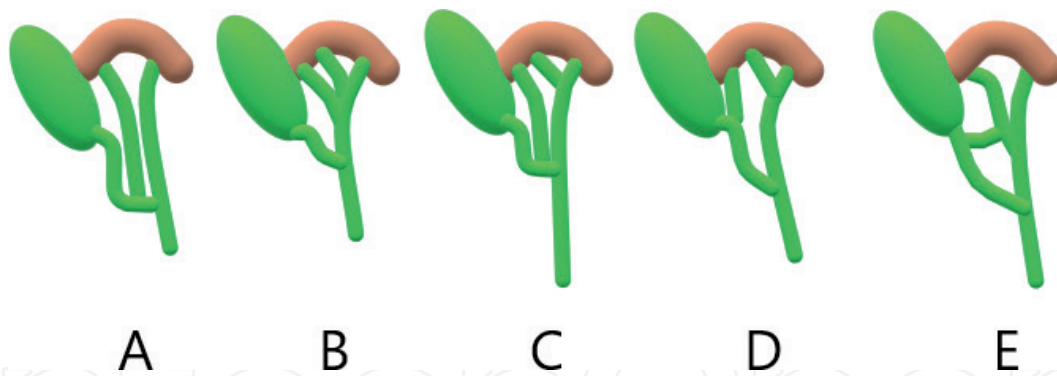


Figure 3. Schematic image of biliary tract variations: A: distal union of the right and left hepatic duct resulting in the absence of CHD; B: accessory hepatic duct joining left hepatic duct; C: accessory hepatic duct joining distal cystic duct; D: accessory hepatic duct joining proximal cystic duct; E: accessory cystic duct joining right hepatic duct.

2.3.2 Arterial variations in hepatocystic triangle important for gallbladder surgery

The right hepatic artery (RHA) after originating from the proper hepatic artery crosses the common hepatic duct posteriorly in 85% of cases and in 15% either RHA or its branches passes anteriorly [3]. For a short distance, RHA runs parallel to the cystic artery before turning upward towards the liver and therefore can be mistaken for the cystic artery [3]. The general rule for minimising such a mistake is that no artery in the Calot's triangle with a diameter of more than 0.3 cm will be a cystic artery [3]. The superior mesenteric artery may give rise to an aberrant right hepatic artery entering the hepatocystic triangle from below and potentially giving rise to the cystic artery in the triangle [3]. In addition to the origins of the cystic artery from the right hepatic artery, there are reports describing the origins from the left hepatic artery with the course anterior to the common hepatic duct, while origins from the common hepatic artery or gastroduodenal artery mean the entry of the cystic artery to the hepatocystic triangle from below [3].

3. Indication for surgical therapy of gallstone disease

3.1 Uncomplicated gallstone disease

Individuals with the gallstone disease have in the majority of cases asymptomatic course mostly continuing throughout their lives and often are diagnosed only incidentally [4].

Therefore, asymptomatic patients do not require surgical intervention and we wait for the symptom appearance [4]. However, cholecystectomy is recommended for asymptomatic patients with an increased risk of gallbladder cancer, like those with gallstones larger than 3 cm, porcelain gallbladder, or with the presence of gallbladder adenomas [4, 5]. In addition, the surgical therapy is recommended in patients suffering from sickle cell disease and spherocytosis, if abdominal surgery is performed due to other concerns, to prevent the formation of pigment gallstones [4].

For patients, who are surgical candidates with uncomplicated gallstone disease with imaging confirmation of gallstones and symptomatic course mostly with the biliary colic, there is a recommendation for an elective surgical therapy [4]. Patients who present themselves to the emergency ward with the acute aggravation

of the biliary colic are treated conservatively with planned surgical intervention after resolution of symptoms due to a lesser risk of complication in elective surgery compared to emergency surgery [4].

3.2 Complicated gallstone disease

Patients with gallstone disease affected by complications such as acute cholecystitis, cholangitis, biliary pancreatitis are recommended to undergo definitive surgical therapy.

In the treatment of acute calculous cholecystitis, it is important to correctly recognise indications for emergency surgery, which are complicated acute cholecystitis with gallbladder gangrene/necrosis, gallbladder perforation, and disease progression despite the medical therapy [6].

If the reasons for emergency surgery are not present, we have to stratify patients benefiting from early surgical intervention and those not profiting from surgery based on their physical status. According to Vollmer et al. [6], the use of the American Society of Anaesthesiologists (ASA) physical status classification is a good option because of its simplicity and ability to stratify patients into low-risk (ASA I-II) and high-risk (III, IV, V) groups with low-risk group patients generally being recommended early cholecystectomy. High-risk group patients are offered nonsurgical therapy, although in case of disease progression and ineffective initial therapy the surgical intervention may be reevaluated [6].

In the group of low-risk patients, the cholecystectomy should be performed as early as possible during the hospitalisation optimally in the first 72 h from the onset of symptoms as it is presumed that the local inflammation worsens with time [6]. Although current Tokyo guidelines as well as World Society of Emergency Surgery guidelines recommend early laparoscopic cholecystectomy also in patients after 72 h, as it is deemed safe because some patients present to hospital already after 72 h from the symptom onset [6]. Patients who have symptoms for longer than 10 days should be planned for delayed cholecystectomy after 6–8 weeks after resolution of the inflammation [6].

In the group of high-risk patients, the initial treatment starts with non-surgical approaches; however, when the disease progresses into gallbladder gangrene/necrosis or perforation or does not respond either to medical therapy or to drainage intervention, the emergency cholecystectomy may be the only option despite the dangers of the surgery [6]. High-risk patients, who handle the acute phase, may be reassessed for delayed surgical intervention and in case of improved physical status may undergo surgery [6]. If the patient's physical status does not improve even after the resolution of the inflammation, these patients are eligible for nonsurgical treatment of gallstone disease [6].

3.3 Gallstone disease in pregnancy

The higher frequency of gallstones in pregnancy compared to non-pregnant patients is based on the physiological functions of hormones released in higher quantities during the pregnancy [7]. Patients with uncomplicated symptomatic gallstone disease with recurrent biliary colic are indicated to undergo cholecystectomy [7]. Although in near term patients suffering from biliary colic, the surgery may be postponed until postpartum [7]. In such cases, it is recommended to perform surgery at least 6 weeks after delivery, but before 3 months after delivery prevent recurrent attacks of biliary colic [7]. Patients with complicated gallstone disease require complex treatment plans. For the patients with acute cholecystitis,

the surgery is a safe indication for the mother and foetus in every trimester [7]. However, increased preterm delivery has been associated with the cholecystectomy in the third trimester in several studies [7].

3.4 Surgical approach towards cholecystectomy

Since the discovery of laparoscopy, this technique has been the mainstay in the surgical approach to gallstone disease regarding uncomplicated gallstone disease as well as complicated acute cholecystitis in low-risk and high-risk groups of patients as well as among pregnant patients unless there is an absolute anaesthetic contraindication [4, 6, 7]. The technical aspects of the laparoscopy in acute cholecystitis may be more demanding on the surgeon's skills; therefore, it is no shame to convert to open cholecystectomy when the surgeon is unable to visualise important anatomical structures with the emphasis on the patient's safety.

4. Patient preparation

The basis for successful and safe cholecystectomy is thorough preoperative preparation with the highest emphasis on the patient's physical status and correct indication for surgical therapy. It is important to assess any patient's comorbidities such as cardiac disease, diabetes mellitus as well as factors potentially complicating cholecystectomy such as previous abdominal surgery in the upper half of the abdomen, inflammation, obesity, and pregnancy.

4.1 Preoperative algorithm

1. Setting a valid indication for surgical therapy based on the patient's clinical status, anamnesis, and paraclinical investigations.
2. Assessment of patient's physical status with his comorbidities resulting in the estimation of ASA level and definition of the patient's fitness for surgery.
3. Assessment of local findings—potential signs of acute cholecystitis, biliary obstruction with the choledocholithiasis, any signs of cholecystoenteric fistula, severe liver diseases such as cirrhosis with portal hypertension, or hepatobiliary malignancy.
4. Assessment of the surgeon's technical skills with adaptation and modification of surgical therapy based on the patient's specific factors.
5. Patient's informed consent with a comprehensive explanation of planned surgery with an explanation of potential complications such as biliary or vascular injuries, the need for conversion from laparoscopic approach to laparotomy, the potential necessity for postoperative ERCP or MRCP.

Eventually, this results in correct indication for surgical or nonsurgical therapy, the timing of the surgery, the type of planned surgery with optimal preoperative preparation (thromboprophylaxis according to Caprini score, antibiotics in indicated cases), and well-informed patient about every step of his procedure with solutions for potential complications [8].

5. Surgical approaches towards gallbladder removal

Cholecystectomy is a common surgical procedure indicated in various gallbladder pathologies. Nowadays, it is one of the most commonly performed abdominal surgeries worldwide [2]. Even though the concepts of safe surgery have been adopted, the iatrogenic injuries to biliary structures are still a worldwide problem. Based on the nationwide databases, the incidence of major biliary duct injuries (BDI) is 0.1% in the case of elective laparoscopic cholecystectomy in comparison with 0.3% in emergency laparoscopic cholecystectomy [9]. Total BDI incidence is 0.4% for elective laparoscopic cholecystectomy compared to 0.8% in emergency laparoscopic cholecystectomy and 0.3% in open cholecystectomy [9]. The ongoing existence of complications in gallbladder surgery even more emphasises the importance of the safe surgery concept.

5.1 Open cholecystectomy

The open cholecystectomy (OC) is currently performed in cases of gallbladder cancer, Mirizzi's syndrome, choledochal cyst, and in cases of sclerotising cholangitis. The incision with its localisation must be adequate for good exploration including the use of intraoperative ultrasonography or radical procedure for cancer.

It is important to emphasise that the conversion from laparoscopic approach to open cholecystectomy is not a surgeon's failure. It seems that the risk is higher in men, patients >60 years old, obese patients, patients with cirrhosis, patients after abdominal surgery in the upper part of the abdomen, patients with severe comorbidities, in case of large gallstones, febrilities, gangrenous cholecystitis, the duration of symptoms >48 h in urgent setting [10]. For the patient's safety, the conversion may be considered in case of the surgeon's inability to perform safe complicated laparoscopic cholecystectomy [10]. However, there is no evidence that the conversion will reduce or avert the risk of biliary duct injury [11]. Conversion to open surgery is an option in any difficult case. The most important focus in a cholecystectomy is the safe removal of the gallbladder and the avoidance of bile duct injuries.

5.2 Laparoscopic cholecystectomy

Nowadays, the state-of-the-art surgical therapy for gallstones is laparoscopic cholecystectomy. Laparoscopy is associated with lower postoperative pain, shorter hospital stay, and shorter recovery period [12]. From the first laparoscopic cholecystectomy in the beginning of the 1990s, this technique has changed the therapy for many gallbladder pathologies. Laparoscopic cholecystectomy is indicated for the therapy of acute and chronic cholecystitis, symptomatic gallstone disease, biliary dyskinesia, acalculous cholecystitis, benign gallbladder tumors. According to a recently published meta-analysis, laparoscopic cholecystectomy is also a safe alternative to open cholecystectomy for early gallbladder cancer (stage Tis—T3) with comparable overall survival and the rate of complications [13].

5.2.1 Technique

Initially, we start with the insufflation of the carbon dioxide into the abdominal cavity until we reach the pneumoperitoneum with the intra-abdominal pressure of 15 mmHg. In conventional laparoscopic cholecystectomy, we continue with the

placement of the multiple ports depending on the surgeon's experience and skills. Surgeon standardly chooses 3 or 4 ports localised supraumbilically (10 mm port), subxiphoidally (10 mm port), and 1–2 ports in the right subcostal region (5 mm port). The key step in the safe gallbladder removal is the achievement of the critical view of safety (more on the topic in part 6) through meticulous preparation and dissection if this can be achieved. Only in this case, the surgeon can continue with the certainty that he/she has identified the cystic artery and the cystic duct. Both structures are then ligated and interrupted. Later on, we continue with the separation of the gallbladder from the gallbladder bed with the use of electrocautery or the harmonic scalpel. To achieve complete haemostasis, some authors recommend lowering intra-abdominal pressure to 8 mmHg for 2 min to spot potential venous bleeding, which can be undetectable with the intra-abdominal pressure of 15 mmHg. The gallbladder is extracted in the retrieval bag. The drainage in the subhepatic region after uncomplicated cholecystectomy is not routinely recommended. In the end, the trocars should be extracted under direct visualisation, and to prevent incisional hernias, some authors recommend fascial sutures in case of ports larger than 5 mm.

5.2.2 Single-incision laparoscopic cholecystectomy (SILC)

Even though the benefits of the conventional multiple ports access laparoscopic cholecystectomy are undeniable, the efforts to further minimise the traumatisation of the abdominal wall continued with the effort to reduce the number of ports. It was shown that laparoscopic cholecystectomy with the use of only one incision is possible in the clinical setting [14]. The limitations of this technique are the difficulties with the triangulation while using linear laparoscopic tools, limited view, and the possibility of the tools' collisions. SILC can be indicated in patients with uncomplicated disease, with BMI $<35 \text{ kg/m}^2$, in whom there is a low probability of conversion either to multiple ports access laparoscopy or open cholecystectomy [15]. However, the role of the SILC compared to conventional LC in day-to-day praxis is debatable based on non-existent clear benefits beyond lower postoperative pain and improved cosmetic effects with no option to clarify the impact on the quality of life [15]. On the other hand, among the disadvantages are the higher occurrence of adverse events with prolonged duration of the surgery and frequent demand for additional port [15].

5.2.3 Common issues in laparoscopic cholecystectomy

The first thing that may compromise our ability to perform safe laparoscopic cholecystectomy may be the problem with the port placement. When we place a supraumbilical port in obese or tall patients in the umbilicus, it can create too low of a view [16]. Another issue with the limitations of fine motor movements may arise when placing the subxiphoidal port too low or not perpendicular to the abdominal wall while creating a form of "port tension" [16]. Tool collisions may happen when we place the surgeon's left-hand port in line with the camera view or the lateral retraction port [16].

The dissection of the gallbladder should be done with the proper incision of the peritoneum, therefore releasing the gallbladder from the liver [16]. A common issue may be with insufficient retraction of the infundibulum inferiorly and laterally and endangering the common hepatic duct or common bile duct by the possibility of an alignment with the cystic duct in the same plane [16]. Important to remember is to use the clips, ligations, or electrosurgical energy on ductal structures only after the visualisation of the regional anatomy [16]. The critical view of safety cannot be achieved unless the bottom third of the cystic plate is fully exposed with adequate dissection of

the hepatocystic triangle and clear identification of the cystic duct and the cystic artery [16]. When the CVS is not achievable, the attempt to perform total cholecystectomy is a risk for the patient and we must utilise a bail-out manoeuvre [16].

5.3 Robot-assisted cholecystectomy

With the introduction of a robot-assisted surgical system, minimally invasive surgery comes to a new era. In 1998, Himpens first reported the robot-assisted cholecystectomy [17]. Since then, the application of the robotic system has been significantly improved, not only for hepatobiliary and pancreatic surgery but also for urological surgery, gynecology, thoracic surgery, and cardiac surgery. The application of daVinci™ robot-assisted surgical platform overcomes the shortcomings of many laparoscopic techniques [17].

5.3.1 Single-incision robotic cholecystectomy (SIRC)

Robot-assisted surgical platform with the single incision has overcome many limitations of single-incision laparoscopic cholecystectomy with bridling the triangulation, quality of view, and movement options [18]. The indication for SIRC is very similar to that of conventional LC. The relative contraindication being the same for SIRC and SILC; however thanks to better triangulation and surgical skills with the robotic platform, SIRC is being more frequently used in patients with higher BMI, acute cholecystitis, and patients with previous abdominal surgeries in the upper abdomen [19].

6. Concept of safe cholecystectomy

Over the years, there have been many methods for reducing the risk of biliary structures injuries while performing cholecystectomy. Fisher's method, in which the surgeon removes the gallbladder from the gallbladder bed and then identifies the cystic artery and cystic duct which are sequentially ligated, is deemed overcome due to 95% penetration of laparoscopy in the gallbladder surgery [12]. The introduction of the Strassberg method in 1995 meant firstly the preparation of cystic artery and cystic duct in a hepatocystic triangle with identification of cystic duct entering the gallbladder infundibulum [20]. This method is currently called the critical view of safety technique (**Figure 4**) [20].

6.1 Critical view of safety

Critical view of safety (CVS) technique is composed of three steps:

1. Identification and visualisation of hepatocystic triangle without the exposition of the common hepatic duct.
2. Visualisation of infundibular part of the gallbladder with the preparation and separation from gallbladder bed (anterior and posterior view).
3. Visualisation of only 2 structures entering the gallbladder before ligation—a cystic artery and cystic duct [21].

This concept is widely accepted and represents the basis of the safe cholecystectomy model to minimise the incidence of iatrogenic biliary ducts injuries [20].

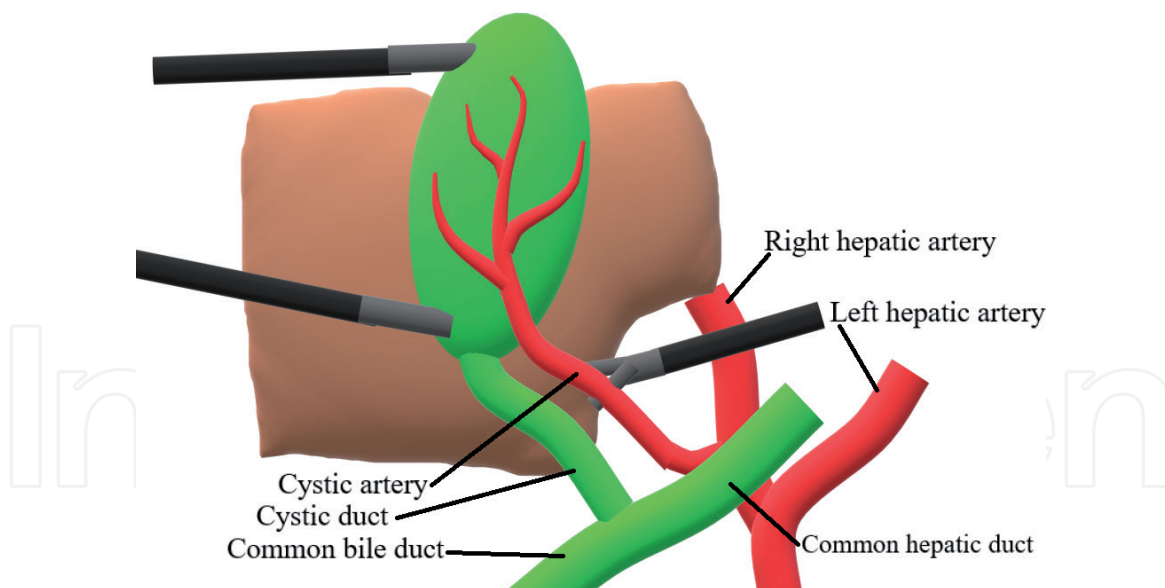


Figure 4.
Schematic image of critical view of safety.

Combination of this method and correct indication for surgery, good preoperative preparation and planning, and meticulous dissection constitute a modern approach towards safe cholecystectomy with reduced risk of biliary structure injury. Due to the scientific verification of reduction in BDIs, the critical view of safety is routinely recommended over other methods [22]. However, CVS cannot always be easily achieved with the most frequent incompleteness in the separation of the infundibular part of the gallbladder from the gallbladder bed. In other cases, the CVS cannot be utilised because of advanced inflammation or scar formation in the hepatocystic triangle due to ongoing or former inflammatory processes [23]. The literature recognised the BDIs to be more frequent in surgeries performed by young residents during the early part of their learning curve in the laparoscopic cholecystectomy. Therefore, it is important for the resident to complete a critical view of safety with the mentoring surgeon to confirm it before ligating any structures [23].

6.2 Bail-out procedures

The concept of CVS cannot be achieved in every case of cholecystectomy; therefore in those situations, the surgeon shall use alternative methods for safe gallbladder removal—the bail-out manoeuvre or another method for cystic duct identification. In the setting of acute cholecystitis, the alternative method “fundus-first” has a lower conversion rate and a lower percentage of iatrogenic injuries to the biliary tree [24]. The technique of subtotal cholecystectomy is used as a safe method with minimal risk of injury to the vascular or biliary structures with low conversion volume due to the resection border being out of the risk zone [10]. However, this method has higher amounts of surgical site infections, re-interventions, and rehospitalisations with a longer length of stay [25]. Conversion to open cholecystectomy is an option in difficult cases as well. However, the conversion to OC does not reduce the risk of biliary duct injury as showed in the results of the Belgian multicentre study [26]. In the study of 1089 patients with acute cholecystitis, 116 patients (11.7%) underwent the conversion to open cholecystectomy with the biliary duct injury of 13.7% (16 patients) [26]. Major BDI was present in 6.0% (7 cases) and three cases of the major BDI occurred after the conversion to OC [26]. These results point out the risk of BDI in high-risk patients undergoing cholecystectomy even in cases when the conversion to open gallbladder removal is performed [26].

Therefore, the subtotal cholecystectomy is the preferred choice in surgeons who has low experience with the open cholecystectomy with the exception of large periprocedural haemorrhage, when the method of choice is open cholecystectomy [26]. In the case of complicated cholecystectomy, the intraoperative cholangiography may be a useful method for the identification of anatomical structures and abnormalities with the risk reduction of BDI, although the disadvantage is the need for access to the biliary tree. Another option may be the use of perioperative ultrasonography, which, however, necessitates the need for proper ultrasonography training and knowledge among surgeons.

7. Intraoperative cholangiography and common bile duct exploration

7.1 Intraoperative cholangiography

Intraoperative cholangiography (IOC) can be used intraoperatively for the identification of choledocholithiasis and for visualisation and identification of biliary tree anatomy. The common use of this technique is currently not recommended because of insufficient reduction in complication rate and BDIs during laparoscopic cholecystectomy [27]. The BDIs can appear even in patients in whom the IOC was performed, because of potentially incorrect interpretation of the findings [28]. However, it may be recommended in patients with difficult biliary anatomy and patients, in whom we are unable to perform critical view of safety or there is a perioperative suspicion of a BDI [28]. Importantly, the identification of BDIs with IOC may lead to earlier recognition with a quick therapeutic approach.

Alternatively, the use of indocyanine green fluorescence cholangiography (ICG-C) may be a good option for visualisation of the biliary tree [29]. This method has been suggested by some studies and proved to be effective in acute and chronic gallbladder diseases and in cases, where IOC cannot be used [30].

7.2 Common bile duct exploration

There is an ongoing controversy about an ideal solution for patients with gallstones and bile duct stones. Historically, the method of choice was the open cholecystectomy with the common bile duct exploration (CBDE), which was replaced due to the progress in the laparoscopic and endoscopic methods. With the improvement of the ERCP, the standard of care for patients with cholecystolithiasis and choledocholithiasis became the preoperative ERCP with the endoscopic sphincterotomy and extraction of the choledocholiths with the subsequent laparoscopic cholecystectomy [31]. It is important to say that the open CBDE was the gold standard during the era of the open cholecystectomies for patients in a need of bile duct stones extraction, with the ERCP being used secondarily. The improvements in the laparoscopy lead to a decline in OC and surgeons started to use and rely more on the ERCP to solve the choledocholithiasis. Laparoscopic CBDE is currently an advanced method and in some centres, it is a method of choice. Although some studies have shown the advantages (lower amount of interventions, lower economic burden, shorter length of stay) of the one-stage procedure (LC + laparoscopic CBDE) in comparison with two-stage procedures (pre- or postoperative ERCP + LC), this practice was not generally accepted [32]. Nowadays, the method of choice is two-stage management with the preoperative ERCP and subsequent LC. Even though the ERCP is considered safe, it is a method with high chances of complications with acute post-ERCP pancreatitis being the most common post-ERCP complication with the high economic burden on healthcare systems [33].

Laparoendoscopic rendezvous (LERV) as a combination of laparoscopy and endoscopy is an attractive method in management of patients with cholecystolithiasis and choledocholithiasis. Recent meta-analysis of eight studies compared LERV with two-stage management (preoperative ERCP + LC) in 1061 patients with gallstones and bile duct stones [34]. A total of 542 patients were treated with LERV technique and 519 patients underwent ERCP with subsequent LC. Between the two groups there were no significant differences in the bile duct clearance (OR 2.20, $P = 0.10$), postoperative bleeding (OR 0.67, $P = 0.37$), postoperative cholangitis (OR 0.66, $P = 0.53$), postoperative bile leak (OR 0.87, $P = 0.81$), or conversion to different approaches (OR 0.75, $P = 0.62$) [34]. Total time of surgery was longer in the LERV group (MD = 44.93, $P < 0.00001$); however, the advantage of the LERV technique was lower incidence of postoperative pancreatitis (OR 0.26, $P = 0.0003$) and lower overall morbidity (OR 0.41, $P < 0.0001$) with a shorter length of hospital stay (MD = - 3.52, $P < 0.00001$) [34]. The authors of the meta-analysis concluded the LERV to be equivalent to standard two-stage management of patients with gallstones and bile duct stones [34].

In current practice, there are clear guidelines by the British Society of Gastroenterology recommending the extraction and clearance of the choledocholiths from the CBD [35]. Although, laparoscopic cholecystectomy is a gold standard for gallstone disease, a consensus on the optimal therapeutic approach in the management of bile duct stones has not been reached. Thanks to the improvements in the laparoscopic technique and surgical skills, the single-stage LC + CBDE has shown its benefits and promise. However, the very limitations are based on the necessity of advanced surgical skills with technical demandingness and the availability of the ERCP rule in favour of the two-stage approaches in the majority of centres [36]. The future may lie with the LERV technique, although as a novel therapeutic approach there are still needed further randomised control trials to decide the optimal therapeutic approach for patients with gallstones and bile duct stones.

8. Complications of gallstone surgical therapy

Invasive procedures may be complicated by a number of factors related either to the surgeon and his skillset or patient's characteristics with the clinical findings and anatomical variations. In the case of laparoscopic cholecystectomy, the complications rate varies from 0.5 to 6%:

- Biliary duct injury with the incidence 0.1–0.6%
- Bleeding and vascular injury with the incidence 0.04–1.22%
- Gallbladder perforation 10–30% [37]

Surgeon experience

Incidence of complication is significantly related to the surgeon's experience. Some authors estimated 50 performed laparoscopic cholecystectomies to complete the training in this procedure. However, the end of the learning curve for laparoscopic cholecystectomy is somewhat debatable. Some studies have evaluated the decrease in the bile duct injuries or conversion and complication rates, while others focused on operation time, but the definitive criteria are still being formed [38]. Nonetheless, experienced surgeons have the lowest complication rates; therefore, an increasing number of institutions require proof of fundamental skills in laparoscopic surgery.

Timing of surgery and patients selection

Patients with acute cholecystitis with inflammatory changes have a higher likelihood for a complication during surgery. Also, a higher rate of complications can be expected in patients with chronic cholecystitis with fibrotic changes in the hepatoduodenal ligament and gallbladder fossa. Choledocholithiasis should be revealed before surgery. Patient's history and a series of examinations can refer to the presence of bile duct stones. Performing routine preoperative ERCP is not currently recommended [39]. It is reasonable only in cases of suspicion of common bile duct stones (dilatation of common bile ducts, clinical or laboratory picture of pancreatitis, fever, elevated inflammatory markers, jaundice).

8.1 Biliary duct injury

Clinical manifestation of biliary duct injury (BDI) can be various and it depends on the kind of injury. BDI can run asymptotically in cases of small damages to the biliary tree to acute process in cases of transection or occlusion of the common bile duct. Approximately only 25% of cases of BDI are recognised during laparoscopy and the detailed description of the case is very important [40].

Type A—This group represents leakage from the gallbladder bed, minor hepatic ducts, and cystic duct without damage to the biliary tree (**Figure 5**).

Type B—Occlusion of the aberrant right hepatic duct (**Figure 6**).

Type C—Transection of the aberrant right hepatic duct (**Figure 7**).

Cystic duct drainage into an aberrant right hepatic duct is a variation seen in approximately 2% of patients. Injuries type B and C are usually caused by confusion of the aberrant right hepatic duct with the cystic duct. Patients with type B injury may remain asymptomatic for a long period of time. Right upper quadrant pain, fever, elevated liver enzymes, and markers of inflammation can be signs of cholangitis, and ultrasonography (US) will show dilatation of the right part of the biliary tree. The occlusion leads to dilatation of the right part of the biliary tree, fibrotic changes, and finally to lobar atrophy. Type C injury causes biliary leakage.

Type D—This group of injuries represents mural lesions of the common bile duct without interruption of its course (**Figure 8**). The result of this damage is a biliary leakage and it can progress to a more serious type E injury.

Type E—This injuries involve interruptions of the extrahepatic biliary ducts and depending on the location of the injury, they are divided into five subgroups (Bismuth classification) [39].

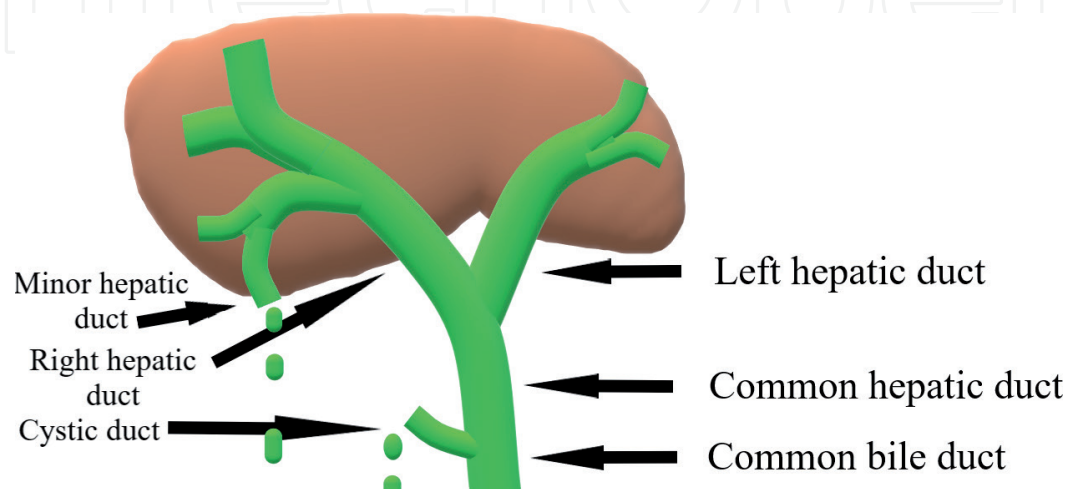


Figure 5. Schematic image of leakage from the gallbladder bed, minor hepatic ducts, and cystic duct without damage to the biliary tree (Type A).

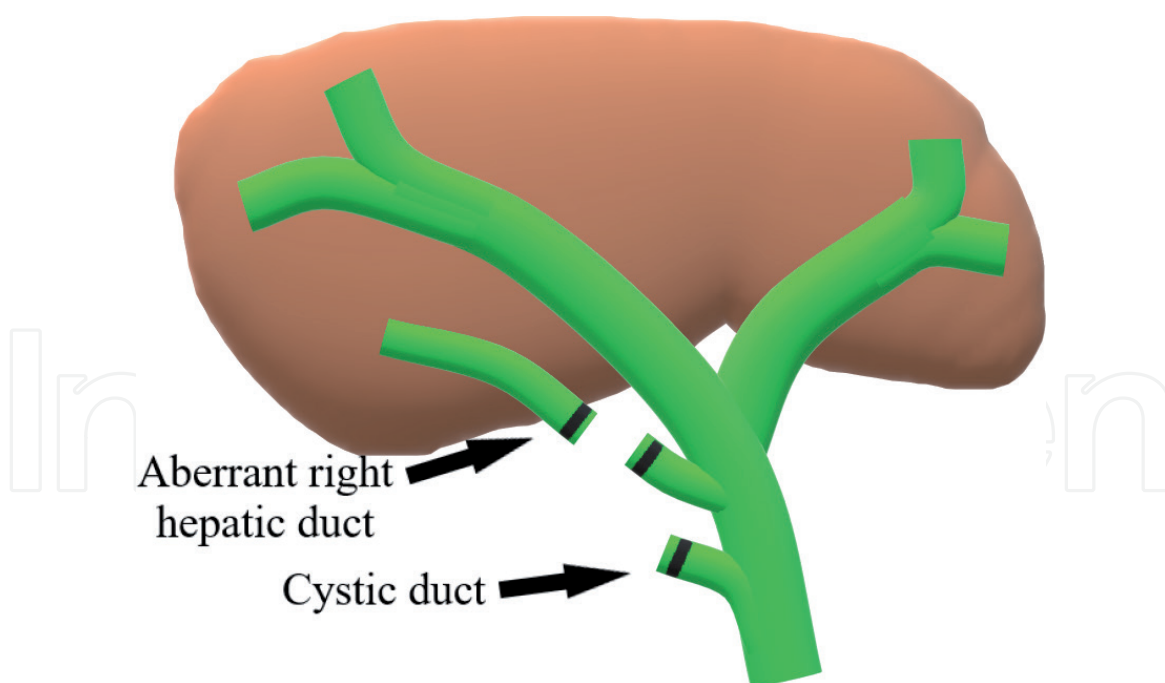


Figure 6.
Schematic image of occluded aberrant right hepatic duct (Type B).

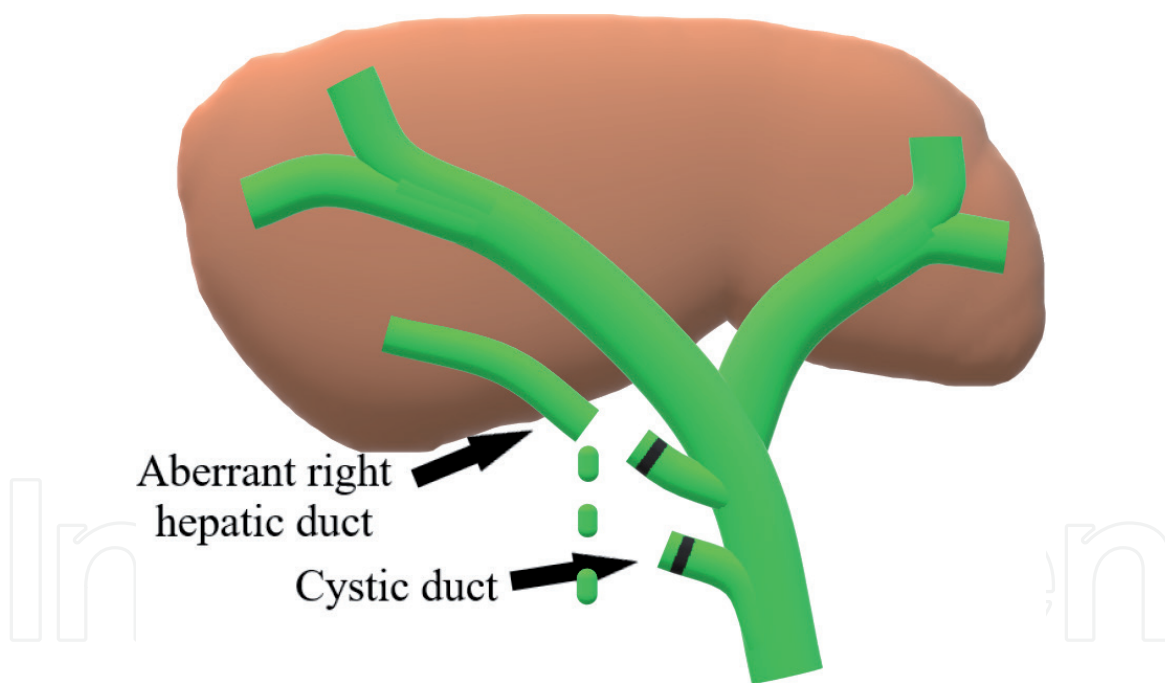


Figure 7.
Schematic image of transected aberrant right hepatic duct (Type C).

E1—(Bismuth Type I)—transection more than 2 cm from the confluence of the right and left hepatic ducts (**Figure 9**).

E2—(Bismuth Type II)—transection less than 2 cm from the confluence (**Figure 10**).

E3—(Bismuth Type III)—transection in the confluence (**Figure 11**).

E4—(Bismuth Type IV)— separation of major duct from the right and left hepatic duct (**Figure 12**).

E5—(Bismuth Type V)—Interruption of the aberrant right hepatic duct (Type C) combined with the injury in the hilum (**Figure 13**).

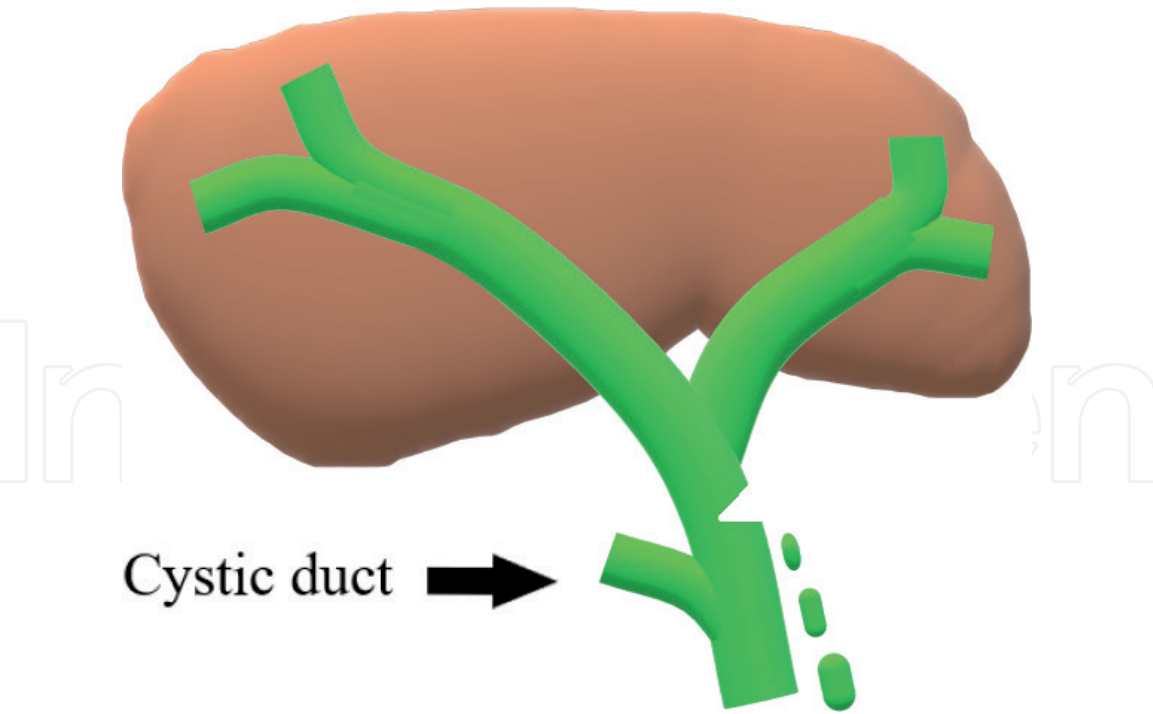


Figure 8.
Schematic image of lesion to the common bile duct without interruption of its course (Type D).

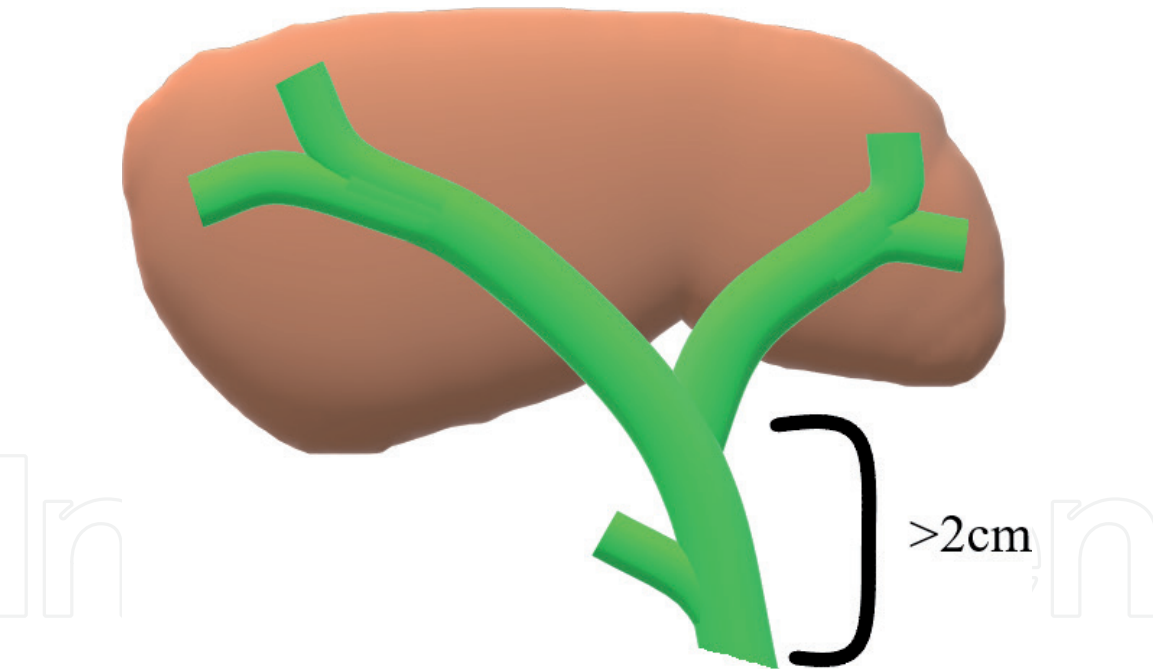


Figure 9.
Schematic image of transected CHD (Type E, Bismuth Type I).

Bismuth classification of BDI was the first scheme published in 1982 [41]. After this classification, other more complex classification systems were proposed. For clinical use, BDI are usually divided into two groups: minor and major injuries.

8.1.1 Diagnosis of biliary injury

Minor BDI are associated with partial lesions without tissue and continuity loss. Major BDI are associated with tissue loss or interruption or occlusion of the main hepatic duct. In a situation when BDI is recognised during laparoscopic surgery,

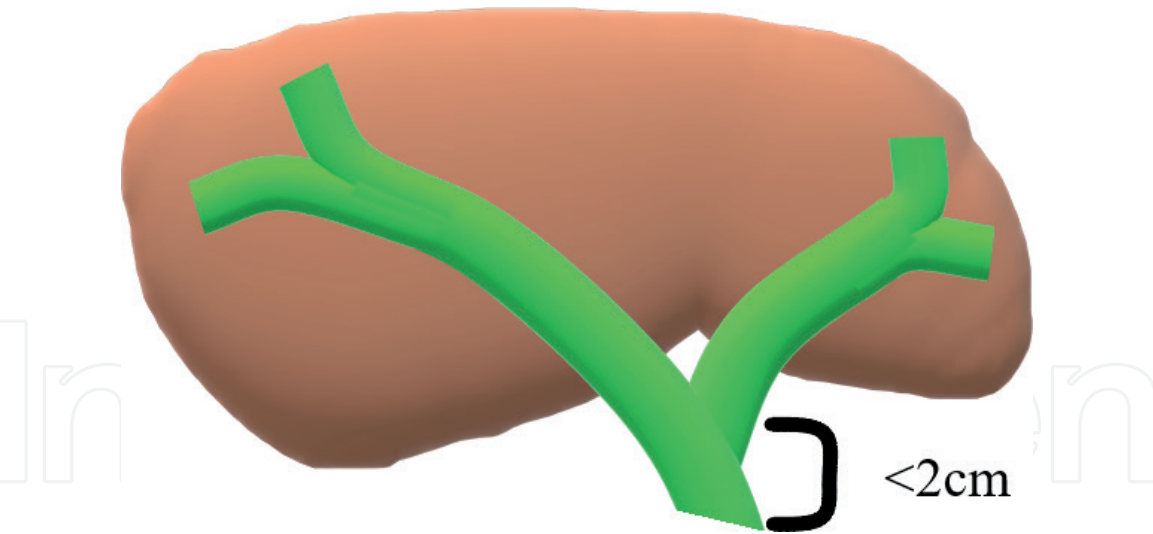


Figure 10.
Schematic image of transected CHD (Type E, Bismuth Type II).

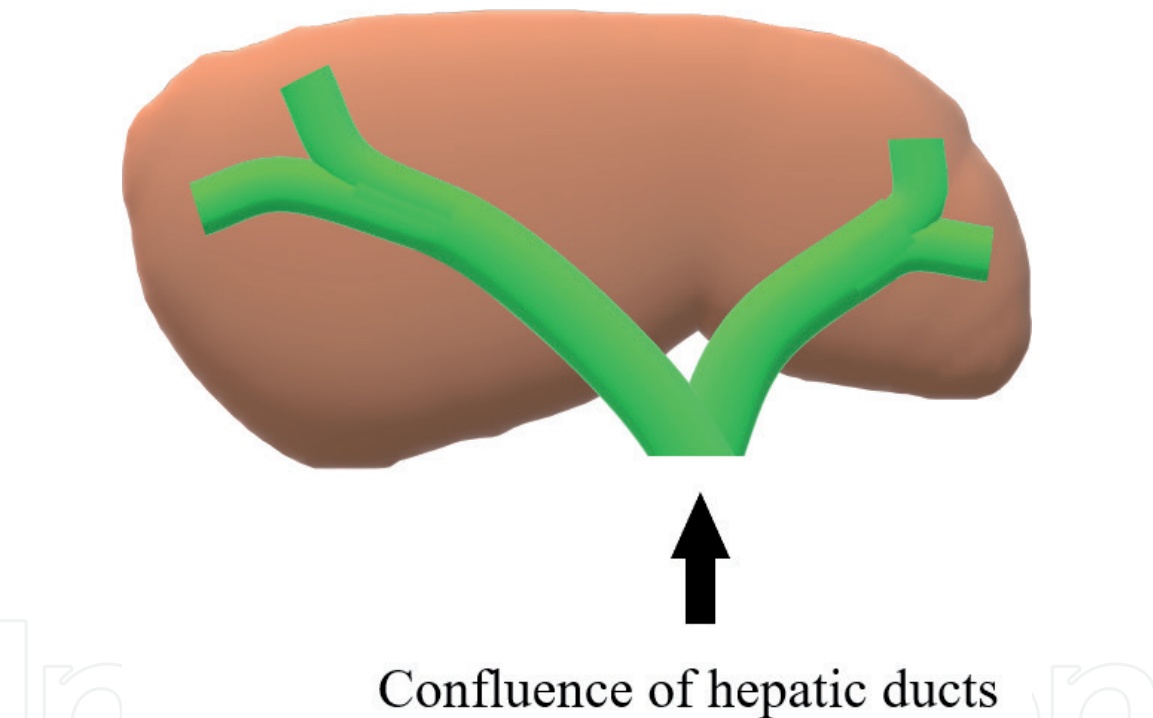


Figure 11.
Schematic image of transected CHD in the confluence (Type E, Bismuth Type III).

conversion to an open procedure and attempt for a repair is recommended only when the surgeon is skilled in advanced biliary surgery. Non-expert immediate attempts for repair are associated with worse outcomes, and they can compromise later revisions; therefore, an intraoperative consultation of an expert is recommended and patients especially with major BDI should be referred to a hepatobiliary centres with multidisciplinary care [39, 41]. External drainage of the subhepatic space is recommended, and a patient should be referred to the centre early because delayed transfers are associated with a higher rate of complications [42].

In case of intraoperative suspicion of BDI or when patients' biliary anatomy is unclear, intraoperative cholangiography may be helpful [28]. Currently, it is not generally recommended to perform routine intraoperative cholangiography because it is not associated with a significant reduction of BDI rates and it can lead to BDI itself because of misinterpretation of patients' anatomy.

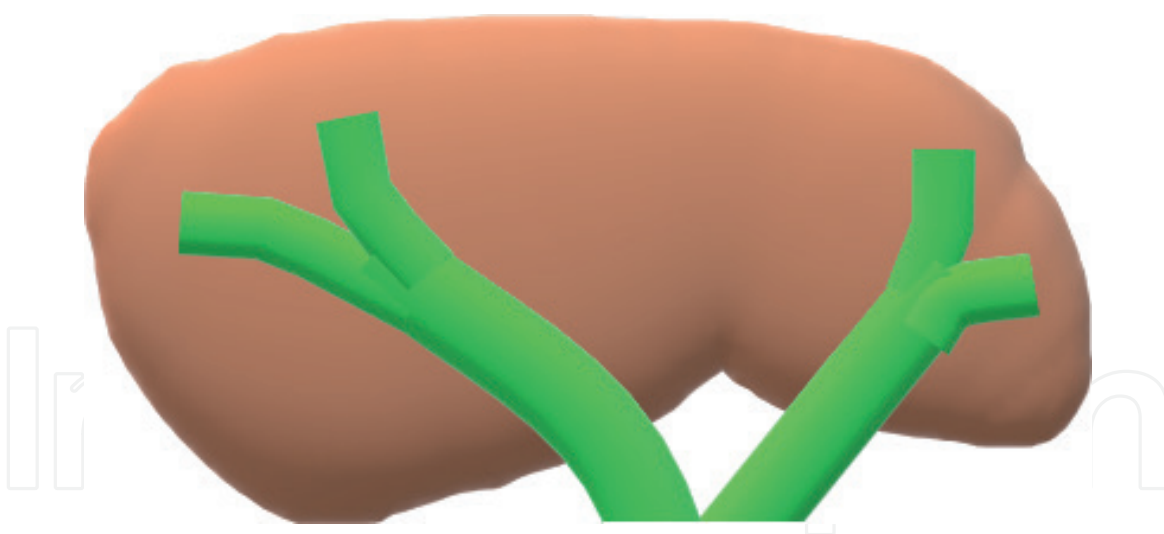


Figure 12.
Schematic image of separated major duct from the right and left hepatic duct (Type E, Bismuth Type IV).

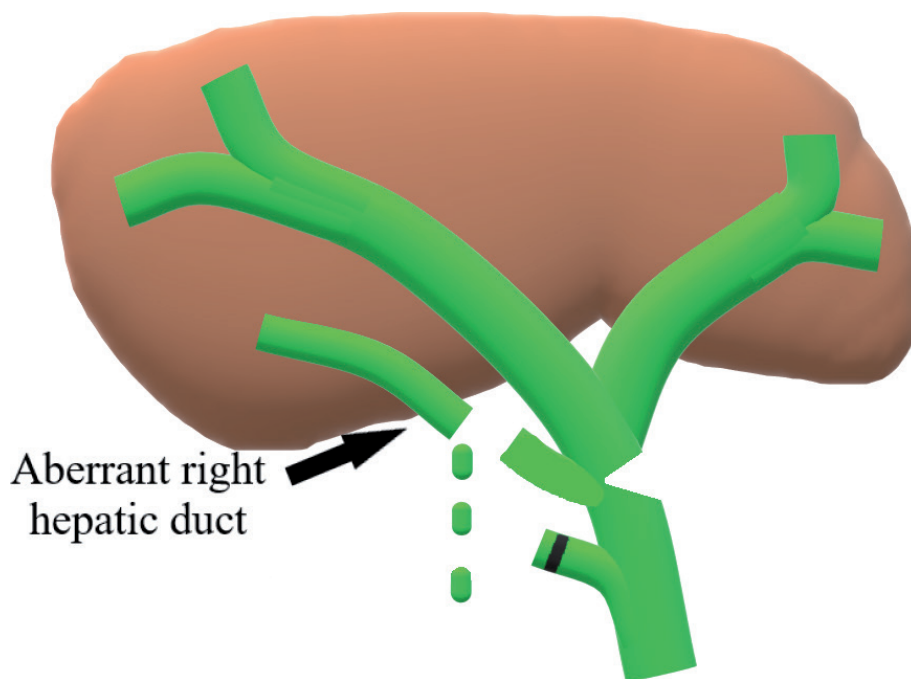


Figure 13.
Schematic image of interrupted aberrant right hepatic duct (Type C) combined with the injury in the hilum (Type E, Bismuth Type V).

8.2 Bile leaks

This group represents biliary injuries types A, C, D, and E.

Type A leak is localised from the cystic duct or the bile duct Luschka [43]. It can be caused by loosen ligature or dislodged clips because of a frail tissue or obstruction of the cystic duct remnant.

Bile duct of Luschka is a minor accessory bile duct that directly enters the gallbladder in the bed. Clinically, significant leakage from the duct after cholecystectomy is not very common.

Types C and D leaks are related to BDI to aberrant and main ducts.

Clinical presentation depends on the extent of the lesion. Minor lesions with small perihepatic collections may remain asymptomatic for a long time or may resolve spontaneously. Major lesions are followed by massive biliary leakage and affected patients are usually symptomatic. Typical symptoms are abdominal pain, bilious collections or bilious ascites, fever. In this case, jaundice is a variable sign because the

serum level of bilirubin can be just slightly elevated. Leucocytosis and elevated serum levels of alkaline phosphatase and gamma-glutamyl transferase are common [39].

If subhepatic drainage during cholecystectomy is performed, bile leakage is usually obvious and the extent of the lesion can be indirectly estimated.

8.2.1 Radiologic examinations and management

Transabdominal ultrasonography (US) is the basic examination that can describe perihepatic fluid collections and the biliary tree diameter. If the US finding is unclear and the symptomatology is worsening, the CT may be helpful to detect free intraperitoneal fluid or associated vascular injury (triphasic CT) [44].

Large collections or free peritoneal fluid of larger volume can be percutaneously drained and examined for assessment of bilirubin levels. It is recommended to take a sample for microbiological examination and in case of clinical and laboratory proof of sepsis development (elevated inflammatory markers), empiric antibiotic treatment is reasonable, particularly in patients with a history of biliary infections and preoperative ERCP and stenting [44].

Bile leakage can be verified by biliary scintigraphy with hepatobiliary iminodiacetic acid scan (HIDA). It is very sensitive in the diagnosis of an ongoing bile leak, though it cannot anatomically localise the site of the leakage. Major leaks can be obvious on early scans, but if early scans are negative, delayed scans after 3 h from tracer injection are recommended [45].

MRCP is a non-invasive method that can be used for the diagnosis of bile leak and localisation of the leak site. It is particularly important in the case of hilar injury [46].

ERCP is an examination that can determine the side of the BDI and offers a possibility of the insertion of the biliary stents. Stenting across the ampulla can solve the majority of BDI types A and D and reduce the pressure in the biliary tree [39]. Sphincterotomy may be performed without stenting; however, it is recommended in cases of biliary obstruction because of choledocholithiasis [39].

In cases when a minimally invasive approach does not solve patients' state, if there is biliary peritonitis and evidence of progressive sepsis, an operative exploration and washout are recommended [44].

In type A injuries, stents can be removed endoscopically usually after 2 weeks if there is no ongoing biliary leak on ERCP [39]. In types C and D injuries, repeated HIDA scans are recommended after 2–4 weeks after stent insertion and stents can be removed if there is no leak on a follow-up ERCP [39]. If the leak persists, stents can be replaced or sphincterotomy can be performed to facilitate the bile flow [39]. Patients with type D injuries require close follow-up due to stricture development or progression to type E injuries in case of larger defects of the biliary wall [39]. Also, endoscopic treatment is less effective in the type C injuries because the aberrant right hepatic duct is disconnected from the proximal part of the biliary tree [39].

Occlusive BDI of the right hepatic bile duct usually leads to segmental cholestasis, fibrosis, and right lobar atrophy. It can be asymptomatic but some patients can suffer from cholangitis or hepaticolithiasis. US and CT may show dilated duct of the right part of the liver with focal atrophy of the liver tissue. ERCP and MRCP will show the site of the obstruction of the right hepatic duct. The treatment of this BDI is surgical. In case when fibrosis and atrophy are not advanced, a hepaticojejunostomy should be performed. Significant atrophy may require resection.

8.2.2 Transections of common hepatic duct

Type E injuries are localised at the common hepatic duct and are the most serious. Transections of the common hepatic duct are usually recognised at the time of

surgery, because of a biliary leak. If there is only a limited mural lesion of the common bile duct, placing a T-tube drain could be a solution. Primary repair attempts should be avoided, especially in case of normal diameter of the common hepatic duct and tissue loss because the probability for breakdown is high and it can lead to bile duct strictures during the healing process [44]. These attempts, especially if they are performed by an inexperienced surgeon, can make the future revisions more difficult [44]. Significant damage of the common hepatic duct is preferably solved by hepaticojejunostomy [44].

Clinical symptoms depend on the nature of an injury. Occlusive injuries lead to jaundice development and elevated liver function tests. Radiological examinations will show diffuse dilatation of intrahepatic bile ducts, and ERCP will verify complete obstruction of the common hepatic duct. In order to decompress the intrahepatic bile ducts, percutaneous transhepatic drainage (PTD) and percutaneous transhepatic cholangiography (PTC) should be performed. Both liver lobes have to be drained and it can require placing percutaneous drains to both intrahepatic parts of the biliary tree. In cases of strictures due to inappropriately placed clips or ligatures, ERCP with the dilatation and stent insertion may be helpful. Endoscopic treatment is not very effective in cases of complete occlusion and if the length of the stricture is longer than 1 cm. The treatment of choice is surgery and hepaticojejunostomy Roux-en Y [44, 47].

8.3 Bleeding and vascular injury

Bleeding from the gallbladder bed is not a rare complication, especially in cases of fibrotic changes in chronic cholecystitis. If laparoscopic attempts for bleeding control fail, it usually requires immediate conversion and ligation [48].

Arterial bleeding is usually caused by the cystic artery transection and can be controlled by clipping, but a surgeon must avoid injury to the right hepatic artery. Injuries of the right hepatic artery require a high level of technical expertise, and the efficiency of reconstruction is questionable. Many right hepatic artery injuries remain unrecognised because its interruption is usually well tolerated [44].

Bleeding from trocar sites should be avoided with direct visualisation after removal.

8.4 Bowel injuries

Bowel injuries are a rare complication. If the bowel injury is recognised intraoperatively, it must be unconditionally repaired. Unspotted bowel injuries may lead to sepsis development after the procedure and require broad-spectrum antibiotic treatment and laparotomy for reparation. Clinical symptoms involve abdominal pain, hypotension with tachycardia with the laboratory picture of leucocytosis or leucopenia, and elevated serum inflammatory markers. In cases when clinical symptoms are mild, a patient does not develop sepsis and an adequate drainage can be achieved, management can be continued as for controlled enterocutaneous fistulas [39].

9. Conclusion

Nowadays, the laparoscopic cholecystectomy is the state-of-the-art surgical therapy for gallstones disease. The primary concept is the safety of the patient; therefore, the surgeon must be aware of the anatomy variations and has to be prepared to react to them. The first thing young residents have to learn is the technique

of critical view of safety to reduce the risk of biliary duct injuries. Although we may do every effort to minimise the risks of complications, those will happen nonetheless. Therefore, every surgeon has to be aware of the basics in the management of cholecystectomy complications.

Conflict of interest

The authors declare no conflict of interest.

Author details

Peter Dubovan, Ramadan Aziri and Miroslav Tomáš*
Department of Surgical Oncology, National Cancer Institute in Bratislava,
Slovak Medical University, Bratislava, Slovak Republic

*Address all correspondence to: dr.mirotoomas@gmail.com

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