Iatrogenic bile duct injury: impact and management challenges

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Abstract: Iatrogenic bile duct injuries (BDIs) after laparoscopic cholecystectomy, being one of the most common performed surgical procedures, remain a substantial problem in gastrointestinal surgery with a significant impact on patient's quality of life. The primary aim of this review was to discuss the classification of BDIs, the proposed methods to prevent biliary lesions, the associated risk factors, and the management challenges depending on the timing of recognition of the injury, its extension, the patient's clinical condition, and the availability of experienced hepatobiliary surgeons. Early recognition of BDI is of paramount importance and limiting the diagnosis delay is crucial for an optimal postoperative outcome. The therapeutic management depends on the type and gravity of the biliary lesion, and includes endoscopic, radiologic, and surgical approaches.

Keywords: bile duct injury, laparoscopic cholecystectomy, biliary anatomy, early recognition, management challenge, endoscopic treatment, surgical repair

Introduction
Laparoscopic cholecystectomy (LC) is one of the most frequently performed procedures worldwide in general surgery.1 Annually, more than 750,000 procedures are performed in the US.2 Bile duct injury (BDI) represents the most serious complication of LC, with an incidence of 0.3%–0.7%, resulting in a significant impact on quality of life (QoL), overall survival, and frequent medico-legal liabilities.1–4 The incidence of iatrogenic BDI has significantly gone up since LC became the “gold standard” in the treatment of symptomatic cholelithiasis. It has been demonstrated that the primary cause of BDI is the misinterpretation of biliary anatomy in 71%–97% of all cases.1 Over the years, various classifications of biliary injuries have been proposed and different methods have been described to prevent iatrogenic biliary tract lesions. Early recognition of BDI is of paramount importance. The optimal treatment is influenced by the timing of recognition of the injury, the extent of BDI, the patient’s clinical condition, and the availability of experienced hepatobiliary surgeons. This article aims to discuss the classification and management challenges of iatrogenic BDIs after cholecystectomy.

Classification of BDIs
Before the advent of LC, the most frequent lesion to biliary tract was represented by bile duct stricture, and biliary injuries were classified using the “Bismuth classification”5 according to the level of biliary injury. This classification includes five types of bile duct lesions according to the distance from the hepatic hilus, the level of injury, the involve-
ment of bile duct bifurcation, and individual right sectoral duct. Few years later, Strasberg et al. proposed a new classification, similar to the Bismuth, but incorporating additional biliary injuries seen more commonly in the laparoscopic era, in particular biliary leaks. In the “Strasberg classification”, biliary injuries were stratified form type A to type E, as summarized in Table 1. McMahon et al. proposed another classification by distinguishing major and minor biliary injuries: lacerations under 25% of the common bile duct (CBD) diameter or cystic duct-common hepatic duct (CD-CHD) junction were considered as minor injury, whereas transection or laceration over 25% of CBD diameter and postoperative bile duct stricture were classified as major injury. The “Stewart-Way classification” involved four classes based on the mechanism and anatomy of biliary injury, as shown in Figure 1. This classification arose from the analysis of operative reports, providing the human mistakes and cognitive processes involved in the mechanisms of BDIs. Class I injury occurs in two ways: 1) either the CBD is mistaken for the cystic duct, but the error is recognized before CBD is divided in 72% of cases, or 2) an incision made in the cystic duct for the cholangiogram catheter is unintentionally extended into the CBD (28% of cases). Class II injuries consist of lateral damage to the CHD with resultant stricture and/or leak. This type of injury occurs when clips or electro-cautery are used too close to the CBD, mainly in cases where visibility is limited due to severe inflammation or excessive bleeding. Class III injuries are the most common (about 60% of cases) and involve complete transection of the main bile duct, which always includes the CD-CHD junction. Class IV injuries include transection or leak of the right hepatic duct (RHD) or posterolateral sectoral duct, often combined with injury to the right hepatic artery.

The “Amsterdam classification” proposed by Bergman et al. in 1996 is also very commonly used in many articles, especially among endoscopists. This classification includes four types of ductal injury: type A with leakage from cystic ducts or peripheral hepatic radicles, type B presenting as major bile duct leakage, type C showing an isolated ductal stricture, and type D with complete transection of the bile duct.

For an easy reading, we have chosen the Stewart-Way classification system in this manuscript, as it better describes the mechanisms of biliary lesion during LC, including also concomitant vascular injuries.

**Prevention of iatrogenic BDI**

Over the years, various methods have been proposed and described in the scientific literature to prevent iatrogenic biliary tract lesions. They are summarized in Table 2. The “critical view of safety (CVS)” technique was introduced by Strasberg in 1995 and it is considered the gold standard to perform a safe cholecystectomy with identification of biliary structures during dissection. Three criteria are required to achieve the CVS: 1) the hepatocystic triangle must be cleared of adipose and fibrotic tissues; the CBD and CHD must not be exposed; 2) the lower third of the gallbladder must be separated from the liver bed to expose the cystic plate; and 3) two and only two structures should be seen entering the gallbladder. CVS was conceived not as a way to do LC but as a way to avoid biliary injury.

In such cases, some surgeons prefer performing the *infundibular method* in order to work very close to gallbladder

<table>
<thead>
<tr>
<th>Bile duct injury</th>
<th>Bismuth</th>
<th>Strasberg</th>
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<tbody>
<tr>
<td>Cystic duct leak or leaks from small ducts in liver bed</td>
<td>–</td>
<td>A</td>
</tr>
<tr>
<td>Occlusion of an aberrant RHD</td>
<td>–</td>
<td>B</td>
</tr>
<tr>
<td>Leak from an aberrant RHD</td>
<td>–</td>
<td>C</td>
</tr>
<tr>
<td>Lateral injury to CBD (&lt;50% circumference)</td>
<td>–</td>
<td>D</td>
</tr>
<tr>
<td>CHD stricture, stump &gt;2 cm</td>
<td>Type I</td>
<td>E1</td>
</tr>
<tr>
<td>CHD stricture, stump &lt;2 cm</td>
<td>Type II</td>
<td>E2</td>
</tr>
<tr>
<td>Hilar stricture with preserved biliary confluence</td>
<td>Type III</td>
<td>E3</td>
</tr>
<tr>
<td>Hilar stricture with involvement of confluence</td>
<td>Type IV</td>
<td>E4</td>
</tr>
<tr>
<td>Stricture to an aberrant RHD and to CHD</td>
<td>Type V</td>
<td>E5</td>
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**Table 1 Bismuth and Strasberg classification**

infundibulum, reducing the risk of biliary injuries, but care
should be taken with “hidden cystic duct” syndrome which
presents a deceptive appearance of a false infundibulum that
misleads the surgeon into identifying the CBD as the cystic
duct.11 The “antegrade dissection or fundus first/dome-down
technique” represents a way of dissection from the gall-
bladder fundus up to the infundibulum away from Calot’s
triangle.12 In this way, the gallbladder is left pedunculated by
the cystic artery and cystic duct, which can be clipped and
divided in turn, reducing the risk of biliary lesions. Another
easy, safe, and definitive operation for the “difficult gallbladder”
is described and has been termed “subtotal or partial
cholecystectomy”,13 consisting in leaving the posterior wall
of the gallbladder attached to the liver and securing the cystic
duct at its origin from within the gallbladder.

Different anatomic landmarks have been described:
among them, in 1924, Henri Rouvière, a French surgeon,
described a 2–5 cm sulcus running to the right of liver
hilum, anterior to the caudate lobe, and usually containing
the right portal triad or its branches.14

<table>
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<th>Table 2 Summary of proposed methods to prevent bile duct injuries</th>
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<tr>
<td>• Critical view of safety (CVS) method</td>
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<tr>
<td>• Infundibular technique</td>
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<td>• Antegrade dissection</td>
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<td>• Subtotal cholecystectomy</td>
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<tr>
<td>• Anatomic landmarks:</td>
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<tr>
<td>o Rouvière’s sulcus</td>
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<tr>
<td>o Calot’s node</td>
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<tr>
<td>o B-SAFE method</td>
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<tr>
<td>• Intra-operative cholangiography (IOC)</td>
</tr>
<tr>
<td>• Laparoscopic ultrasound (LUS)</td>
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<tr>
<td>• Near-infrared fluorescent cholangiography (NIRF-C)</td>
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<tr>
<td>• Conversion to open surgery</td>
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</table>

Note: B-SAFE: B, bile duct; S, sulcus of Rouvière; A, hepatic artery; F, umbilical fissure; E, enteric/duodenum.

The opinions about the “routine” or “selective” use of IOC
still represent a matter of debate.1,19

“Laparoscopic ultrasound (LUS)” was shown to provide
highly sensitive mapping of the extra-hepatic biliary anatomy
but the difficult learning curve and the lack of randomized
controlled trials have reduced its use in clinical practice.21,22

One of the latest innovations in minimally invasive tech-
nology is fluorescence image-guided surgery; “near-infrared
fluorescent cholangiography (NIRF-C)” represents a novel
intra-operative imaging technique that allows a real-time enhanced
visualization of the extrahepatic biliary tree by
fluorescence.23–25 NIRF-C well represents a useful method to
identify the CVS with the aid of real-time fluorescent vision
with a perfect combination between surgical anatomy and
technical innovation, as shown in Figure 2.26

In some difficult situations, the opinion of a surgical
colleague in vicinity during operation may also represent a
valid alternative, the so-called “colleaguerography”, in place
of IOC or other methods, as proposed by some authors.27

Despite the plethora of publications and debates, there is
still no consensus as to which method is the best to prevent
BDIs during LC. Recently, highest consensus was achieved
on the importance of the CVS and NIRF-C, as well as ante-
grade dissection or fundus first/dome-down technique and
partial cholecystectomy as alternative techniques.28,29

A general recommendation is that in all cases of complica-
ted cholecystectomies, the surgeon must not hesitate when
considering conversion to open approach because there is
no substitute for experience and caution in biliary surgery.

**Risk factors**

There are several risk factors which can contribute to the
iatrogenic injury of the biliary tract: anatomical factors;
patient-related factors; and factors related to the gallbladder
disease, the surgical technique, and the surgeon. Among the
anatomical factors, the numerous anatomical variants of the
biliary tract represent a possible cause of iatrogenic lesion,
for example, the different variants of the cystic duct, such
as short cystic duct, cystic duct running parallel to the CBD,
anomalies of the CD-CHD junction, presence of the hepato-
cystic duct, accessory cystic duct, the existence of aberrant
bile ducts (eg, Luschka duct).30 Among the patient-related
Clinical presentation

Clinical presentation depends essentially on the extent and type of iatrogenic lesion, if this is not discovered intraoperatively. The presence of a possible biliary leak can start with non-specific symptoms, such as nausea, vomiting, bloating, widespread abdominal pain, general discomfort, and anorexia. Rarely, the patient presents the clinical picture of biliary peritonitis, despite large amounts of bile in the abdomen. The evolution of biliary leak is very subtle, because of the presence of these vague symptoms. Patients with strictures at level of the CBD, in cases where the CBD is mistaken for the cystic duct, will present the classic Charcot’s triad with pain in the right hypochondrium, fever, and jaundice. A general recommendation is that any alteration in the normal postoperative course after LC must suggest a possible damage to the biliary tract. For these reasons, a careful clinical evaluation of patients is essential. A delay in the diagnosis is crucial for the postoperative outcome.

Timing of recognition

Early recognition of BDI is of paramount importance. Intraoperative recognition should typically prompt immediate surgical repair as this confers the best outcomes; however, <25%–30% of BDIs are recognized during operation and not all surgeons perform an intra-operative cholangiography.36,37 If the surgeon is inexperienced, an intra-abdominal drain should be placed, and the patient should be immediately transferred to a high-volume hepatobiliary center. There are several data suggesting that these injuries are best managed by a surgeon with expertise in biliary reconstruction with better outcomes.37-39 There are several factors that lead to a recognition of intra-operative lesion, but the most important is the surgeon’s awareness to suspect and/or evaluate for a BDI. Diagnosis often occurs in the immediate postoperative period (within 6 weeks post-intervention) or, in some cases, later (over 6 weeks). A careful clinical evaluation helps for a correct diagnosis. The appearance of persistent or abnormal abdominal pain in the right hypochondrium, the leakage of bile from drainage (if placed during surgery), a picture of biliary peritonitis, and the appearance of fever and jaundice with increased liver function tests are all elements supporting a diagnosis of any iatrogenic lesion of the biliary tree. Radiologic investigations should be obtained for the correct identification of the damage, its extension, and gravity and to plan therapeutic strategies. Abdominal ultrasound represents the first diagnostic tool aimed at finding any liver collections, dilatation of the CBD, and any associated vascular lesions.40 The abdominal computed tomography (CT) scan is the principal investigation that allows to define the possible presence of focal intra- or peri-hepatic fluid collections, ascites, biliary obstruction with upstream dilatation, or long-term sequelae of a long-standing bile stricture, such as lobar hepatic atrophy or signs of secondary biliary cirrhosis. The CT scan also allows to identify any associated vascular lesions, such as to the right hepatic artery.

Magnetic resonance cholangio-pancreatography (MRCP) represents the “gold standard” for the complete morphological evaluation of the biliary tree as it offers detailed information about the integrity of the biliary tract.41,42 MRCP can also be done with a contrast agent (a gadolinium-based contrast agent, the gadoxetic acid and its salt, gadoxetate disodium), and it is much more informative in bile leaks than plain MRCP.42 The use of a contrast agent during MRCP allows detection of active bile leakage by direct visualization of
contrast material extravasation into fluid collections in addition to demonstrating the anatomical site of the leakage and the type of BDI. For example, in Figure 3 cystic duct leak was demonstrated at MRCP after gadoxetic acid injection. In the same way, hepatobiliary scintigraphy may confirm the presence of an active biliary leak with the progressive accumulation of the radiotracer inside the peritoneal cavity, but this examination is much less reliable. However, if fluid collection is found in ultrasound, CT, or MRCP, an abdominal drain should be placed right away under radiological guidance in order to improve patient’s clinical condition (peritonitis, sepsis, tissue repairing). If there is a delay of more than a week in operative treatment of Stewart-Way Class III or IV injuries, there should be a timeout for 2–3 months before operation. In this time frame, the patient needs to be stabilized and optimized for surgery. An optimal control of any intra-abdominal fluid collection, inflammation, and infection is essential, and is best achieved with percutaneous drainage.37

In the postoperative period, re-laparoscopy can identify the biliary injury, drainage of any intra-abdominal collection, and exclusion of injury to other surrounding organs, which can lead to the decision between conservative management and early or late definitive surgical repair.45

There is no role for explorative laparotomy, as this is associated with increased morbidity and mortality.

**Therapeutic management**

The endoscopic retrograde cholangio-pancreatography (ERCP) examination has an important therapeutic role in cases where a conservative therapeutic approach is preferred based on the type and extent of the biliary lesion (cystic duct leaks, Stewart-Way Class I injuries, and most Class II injuries).

Cystic duct leaks are well managed conservatively; the endoscopic procedure allows to perform a sphincterotomy with the aim of reducing the pressure in the biliary tree and to place a plastic stent or a naso-biliary tube to limit or exclude the fistula (depending on the location of the biliary leak). After the right patient selection, the success rate of endoscopic treatment can approach 100% for cystic duct or peripheral radical leaks. Endoscopic sphincterotomy is an effective and cost-effective single procedure with success rate similar to endoscopic sphincterotomy and biliary stenting, as proposed by Rainio et al.44 Self-expanding biodegradable biliary stents have only recently become available in order to avoid second endoscopy with good results.45 The limits of the endoscopic treatment concern the lack of visualization of aberrant or sectioned bile ducts which do not communicate with the CBD (eg, an aberrant RHD), the cases of complete transection of the bile duct, and the difficulty in visualization of possible intra-hepatic proximal leaks. In this specific case, the percutaneous transhepatic cholangiography (PTC) is superior in the definition of the lesion and in the biliary drainage.

Stewart-Way Class I injuries, which are by definition recognized intra-operatively, can be immediately repaired by using fine monofilament absorbable suture. Insertion of a T-tube catheter is rather contraindicated, as extension of the laceration to facilitate T-tube insertion results in worsening and progression of the injury and an increased likelihood of stricture.46

Stewart-Way Class II injuries consist of lateral damage to the CHD with resultant stricture and/or leak. The management of biliary leak requires a multidisciplinary approach with endoscopy and radiological-guided drainage as the first therapeutic options. Stewart-Way Class II injuries with stricture can be treated with multiple plastic stents and self-expanding covered metallic or biodegradable stents, depending on the gravity of biliary lesion.45

Stewart-Way Class III and IV treatment is mostly operative, but even in such conditions Stewart-Way Class III lesions can also be treated mini-invasively by endoscopic and radiologic extra-anatomical rendezvous reconstruction.47,48 Fiocca et al48 proposed a combined endoscopic–radiologic rendezvous technique to treat the complete transection of the main bile duct, as it is possible to avoid difficult surgical reintervention that presents some morbidity and mortality.

Class IV injuries that involve a sectoral bile duct without transection of the duct can often be managed non-operatively, with drainage and stenting via either ERCP or PTC, with good outcomes in many cases.49–53 Class IV injuries involving

**Figure 3** (A) Axial three-dimensional MRCP sequence showing a small fluid collection in the gallbladder fossa (white arrow). (B) T1-weighted hepatobiliary acquisition (after gadoxetic acid injection) demonstrates opacification of the small fluid collection suggesting a biliary leak from the cystic duct.

**Abbreviation:** MRCP, magnetic resonance cholangio-pancreatography.
transection of the bile ducts require reconstruction of the duct (either the RHD or a right sectoral duct) into a defunctionalized Roux limb.

With regard to reparative surgery, there are some basic rules, and the difficulty in repairing damage derives from both the size and caliber of the bile duct and from local inflammatory and sclerotic changes. The timing of the operation is an extremely important factor in the repair of the lesion; therefore, an early identification of the lesion plays a key role. In case of partial or complete transection of the CBD, it is possible to perform a direct end-to-end suture if the distal choledochus is free and without tension. It is also preferable to protect the suture by inserting a Kehr T-tube, as shown in Figure 4. There is also a second type of T-tube available for biliary drainage, the so-called internal Y-drainage,

which involves the insertion of the two short branches into both the right and left hepatic ducts, splinting of the anastomosis, and conducting of its long branch into the duodenum by the papilla of Vater. This tube can be removed endoscopically after healing of the end-to-end ductal anastomosis. Moreover, it was suggested as the drainage of choice in end-to-end ductal anastomosis. In case of impossibility to perform a direct suture or in cases of severe biliary strictures, a biliodigestive suture or in cases of severe biliary strictures, a biliodigestive anastomosis is recommended, a Roux-en-Y hepaticojejunostomy in most cases, as demonstrated in Figure 5. If a hepaticojejunostomy cannot be performed due to the presence of dense adhesions with infected and friable tissues, some authors have proposed a combination of endoscopic biliary stenting and pedicled omental patch repair of the bile duct to control bile leak and sepsis as a bridging procedure to definitive hepaticojejunostomy.

In case of strictures involving the bifurcation or left or RHD, bilateral hepaticojejunostomies may be necessary. For many years, biliary repair has been the prerogative of open surgery. Nowadays, the improvement in surgical technology has allowed to perform reconstruction of iatrogenic biliary lesions even by laparoscopic or robotic approaches with good results. In a recent paper, Cuendis-Velázquez et al have demonstrated that the robotic approach is similar to the laparoscopic technique regarding safety and efficacy in attaining primary patency of hepaticojejunostomy for bile duct repair.

Liver resection is very rarely indicated in cases of extensive hepatic necrosis. In a small subset of patients with iatrogenic BDIs, failure of surgical or non-surgical management might lead to acute or chronic liver failure necessitating liver transplantation.

Bismuth and Strasberg classifications do not include concomitant vascular injuries during LC. In the Stewart-Way classification system, the Class IV biliary injuries are frequently associated with concurrent right hepatic artery lesions. The right hepatic artery injuries may present with hepatic abscess, hemobilia, and right hepatic lobe ischemia. Many of these patients require angioembolization for treat-

Figure 4 Trans-Kehr cholangiography after the positioning of T-tube to protect biliary anastomotic suture.
**Notes:** Normal cholangiogram showing opacification of the cystic duct, CBD, common hepatic duct, right and left hepatic ducts, and the duodenum. The biliary tree is free without strictures and there is no evidence of biliary leak.
**Abbreviation:** CBD, common bile duct.

Figure 5 A hepaticojejunostomy was performed for a stricture at biliary confluence after the positioning of T-tube.
ment of hemobilia and drainage of hepatic abscesses, and some require hepatectomy.65–68

Furthermore, some authors have also analyzed the consequences of biliary injuries in terms of patient’s QoL. Flores-Rangel et al69 reported that the QoL of the patients undergoing a biliointestinal derivation due to a biliary injury, independently by surgeon’s experience, is reduced significantly when compared to patients undergoing uncomplicated cholecystectomy. Moreover, Booij et al70 have analyzed the long-term impact of BDIs on QoL and found that BDIs are associated with a significant decrease in patient’s QoL and work-related limitations.

Conclusion

Iatrogenic BDIs represent a serious complication which can be brought on by cholecystectomy. The errors leading to laparoscopic bile duct lesions stem principally from misperception of the biliary anatomy. Any effort toward the reduction of the risk profile of everyday cholecystectomy is appreciated. The key points to successful treatment are characterized by early recognition, control of any intra-abdominal fluid collection and infection, nutritional balance, multidisciplinary approach, and surgical repair by an experienced surgeon in biliary reconstruction.

Disclosure

The authors report no conflicts of interest in this work.

References


