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Review Article

Identification and management of subvesical bile duct leakage after laparoscopic cholecystectomy: A systematic review

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A B S T R A C T

Bile leak is a rare complication after Laparoscopic Cholecystectomy. Subvesical bile duct (SVBD) injury is the second cause of minor bile leak, following the unsuccessful clipping of the cystic duct stump. The aim of this study is to pool available data on this type of biliary tree anatomical variation to summarize incidence of injury, methods used to diagnose and treat SVBD leaks after LC. Articles published between 1985 and 2021 describing SVBD evidence in patients operated on LC for gallstone disease, were included. Data were divided into two groups based on the intra or post-operative evidence of bile leak from SVBD after surgery. This systematic report includes 68 articles for a total of 231 patients. A total of 195 patients with symptomatic postoperative bile leak are included in Group 1, while Group 2 includes 36 patients describing SVBD visualized and managed during LC. Outcomes of interest were diagnosis, clinical presentation, treatment, and outcomes. The management of minor bile leak is controversial. In most of cases diagnosed postoperatevely, Endoscopic Retrograde Cholangio-Pancreatography (ERCP) is the best way to treat this complication. Surgery should be considered when endoscopic or radiological approaches are not resolutive.

1. Introduction

Laparoscopic Cholecystectomy (LC) is one of the most frequently performed surgical procedures in General Surgery. Since its first introduction in 1985 by Erich Muhe[1], it represents the gold standard surgical treatment for gallstones disease with excellent outcomes and low risk of morbidity. However, no surgical procedure is free from possible postoperative complications. Iatrogenic Bile Duct Injuries (BDIs), such as leakages or stricture, are the most fearsome postoperative complications, significantly increasing morbidity and mortality for patients. Moreover, in the beginning of laparoscopic Era, many authors reported that the LC technique's introduction seems to be related to an increased prevalence of BDI until 2%[2], higher than the open cholecystectomy one (0.1%).[3]

Risk factors for Iatrogenic BDIs during LC could be several, depending on the condition of surgery (elective or emergency), tissues inflammatory state (acute or chronic cholecystitis), anatomical features (regular or variant vessels or bile ducts), quality of laparoscopic instruments availability and surgeon expertise. Most of these conditions are intrinsic, non-modifiable risk factors. However, a furthered knowledge of biliary tree anatomy and its variations is essential to decrease the risk of inadvertent injury of bile ducts during hepatobiliary surgery. Over the years, the standardization of the surgical technique and the “critical view of safety” (CVS) method for identifying the cystic duct and cystic artery effectively minimized the incidence of BDI during laparoscopic cholecystectomy.[4]

Wrongly recognition of anatomical structures and/or the presence of anatomical variation of the biliary tree could increase this complication's risk.

According to the site, the diameter, and the bile outflow of the damaged duct, several classifications were designed to categorize

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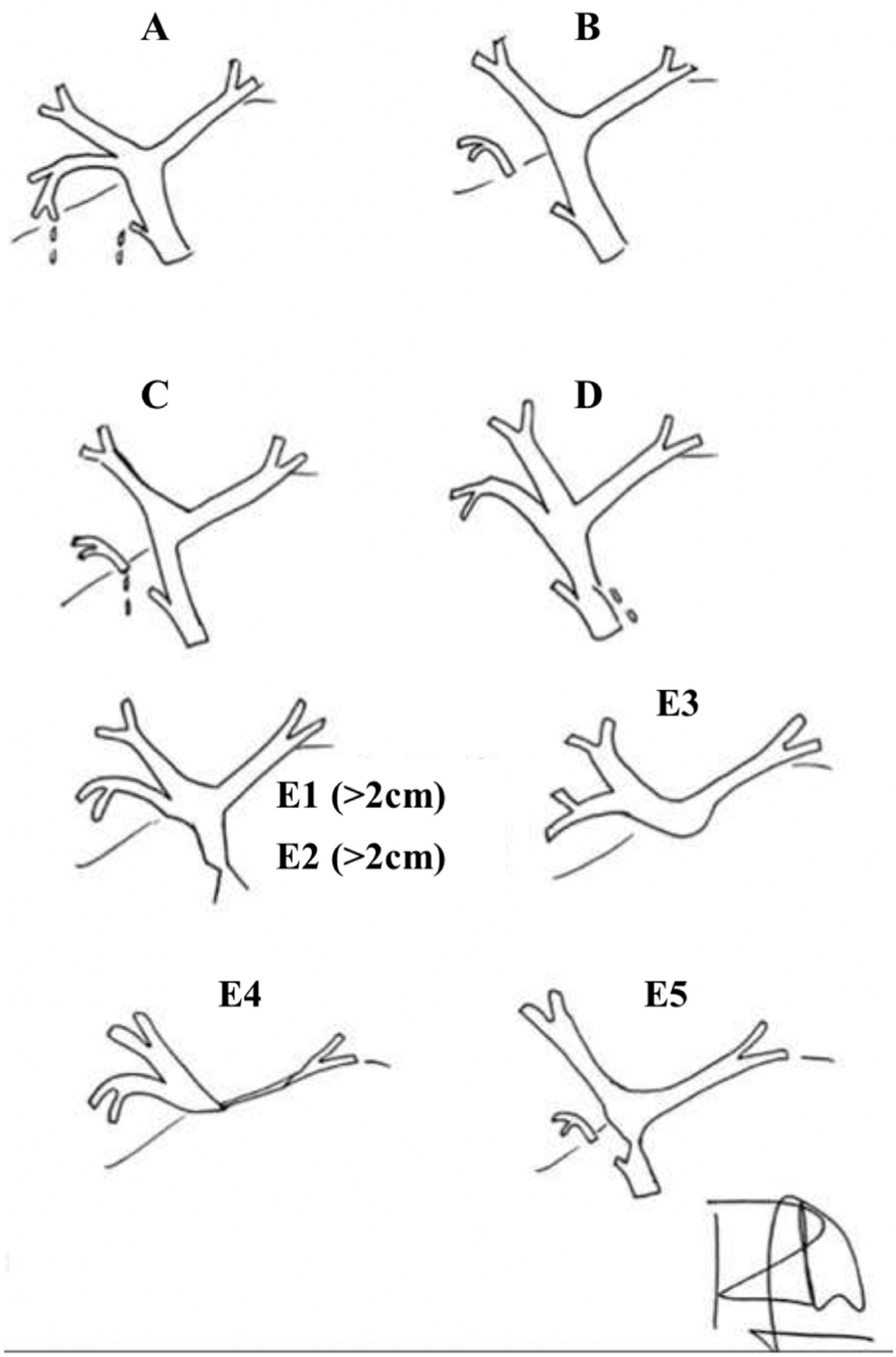

Fig. 1. Classification of laparoscopic injuries to the biliary tract according to "Strasberg classification system". Type A: Bile leak from the cystic duct or liver bed (Subvesical bile ducts) without further injury; Type B: Partial occlusion of the biliary tree, most frequently of an aberrant Right hepatic duct (RHD); Type C: Bile leak from duct (aberrant RHD) that is not communicating with the common bile duct (CBD); Type D: Lateral injury of the biliary system, without loss of continuity; Type E: Circumferential injury of the biliary tree with loss of continuity.

and grade the biliary tree injury severity. The most known is the "Strasberg classification system", which classifies BDIs into the following five categories[5] illustrated in Fig. 1.

Major biliary injuries involve the common bile duct (CBD) and the right and left hepatic ducts (Strasberg type D and E). Generally, major biliary injuries are severe and require surgery management and biliary reconstruction. Strasberg type A, B, and C are considered minor biliary injuries, presenting with various grades of severity depending on the damaged duct's diameter. In most cases, minor biliary injuries can be effectively managed with mini-invasive procedures like endoscopy or interventional radiology.

Subvesical bile ducts (SVBD) are included in the Strasberg type A classification system and represent a common anatomic variation of the biliary tree, with frequent clinical and surgical implications.

Indeed, about 27%[6] of bile leakages are caused by SVBD injury, representing the second cause of minor bile leakage after LC, following leakages from the cystic duct stump. The volume of extravasated bile into the abdominal cavity depends on the caliber of the damaged duct. Usually, bile leak from SVBD tends to be small and often resolves spontaneously without any invasive or not invasive treatments. For that reason, SVBD leakages are classified as "minor" bile duct injuries. However, when the volume of extravasated bile is large, bile peritonitis and sepsis can occur, severely deteriorating the patient's condition. In these cases, delayed diagnosis or management is associated with an increased risk of morbidity, mortality, hospitalization, and poor quality of life.

This review of current Literature aims to clarify SVBD anatomy and summarize incidence, clinical manifestation, and methods used to diagnose and treat SVBD leaks after LC.

2. Methods

This systematic review has been performed according to the PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) statement.[7] Our inclusion criteria were articles published following the introduction of LC[8], article describing radiological identification of subvesical bile ducts, article reporting information about subvesical bile duct leak as an outcome in patients operated on LC for gallstone disease, article describing the treatment of subvesical bile duct leak and full-text English articles.

We conducted a systematic literature search on PubMed, Embase and Scopus for published relevant articles in June 2021 and the key words were "((hepatocholecystic OR subvesical OR luschka OR aberrant OR accessory) AND bile duct) AND cholecystectomy". Original papers, case reports/series, and review articles published between 1985 and June 2021 reporting information about evidence, radiological study, and management of SVBD in patients operated on LC for gallstone disease were considered eligible for the review.

Two independent investigators performed the first screening to exclude duplicates and articles with off-topic titles and abstracts. After the primary screening, a further selection was performed to select those articles in which full-text was available in English. All Full-text available manuscripts were read and analyzed by a single investigator. Articles with insufficient data and/or unrelated topics were excluded.

Data extracted from eligible studies were entered in an Excel spreadsheet (Microsoft) and sorted by authors, year of publication, number of patients reported, radiological examination used to detect the presence of SVBD or HCD, evidence of intraoperative or postoperative bile leak, clinical information, treatment choices, and outcomes.

Finally, patients were divided into two groups. Group 1 included patients with postoperative bile leak from an SVBD injury; Group 2 included patients with pre or intraoperative diagnosis of SVBD in which a postoperative bile leak didn't occur.

3. Results

The literature search resulted in 306 items. After the first screening, 134 articles were excluded because of duplicates or off-topic titles and abstracts. Of 172 selected articles, full-text English available papers were 134. Other 66 papers were excluded because of lack of sufficient data and/or unrelated topics in the full-text. A total of 68 articles met the inclusion criteria and were deemed eligible for inclusion in our final analysis. Studies included are case reports and case series, for a total of 231 patients.

The PRISMA diagram is shown in Fig. 3.

Group 1 includes patients reported with postoperative SVBD leak, analyzing clinical data (time of onset and types of symptoms), methods used to diagnose the site of bile leak, treatment approach, and outcomes (Table 1).

A cohort of 195 patients operated on LC was included. It is important to report that in 5 cases included in this group, the SVBD leak was already identified and clipped during surgery without benefit. In the other cases, the diagnosis was made after surgery following the appearance of clinical signs. Only 38 articles reported the time of onset of symptoms, for a total of 96 patients. Symptoms occurred in the first week after surgery in 62.5% and after seven days from surgery in 37.5% of patients. This information remains not available in 12 papers for a total of 102 patients. The type of symptoms was reported for 87 patients: pain occurred in 93.1%, fever in 74.7%, and jaundice in 67.8% of described cases. This information remains not available in 17 papers for a total of 108 patients.

Table 1
Patients with postoperative subvesical duct leak (group 1).
CT, Computed Tomography; MRCP, Magnetic resonance cholangiopancreatography; PTC, Percutaneous Transhepatic Cholangiography; ERCP, Endoscopic Retrograde CholangioPancreatography.

Group 1	Case reported/total (%)	Successful rate (%)
Time of onset symptoms after surgery		
• < 7 days	60/96 (62,5)	
• > 7 days	36/96 (37,5)	
• NA	99/195	
Type of symptoms		
• Pain	81/87 (93,1)	–
• Fever	65/87 (74,7)	–
• Jaundice	59/87 (67,8)	–
• NA	108/195	
Post-operative diagnosis		
• CT	51/56 (91)	–
• MRCP	2/56 (3,5)	–
• CT + MRCP	2/56 (3,5)	–
• PTC	1/56 (1,8)	–
• Bile discharge from the tube	75/81 (92)	–
• NA	139/195	
Treatment		
• Conservative management	19/180 (10,5)	19/19 (100)
• Percutaneous drainage	14/180 (7,7)	1/14 (7,1)
• ERCP	155/180 (86)	123/155 (79,3)
• Surgery	37/180 (20,5)	32/37 (86,5)
• Exclusive surgery	17/180 (9,4)	17/17 (100)
• NA	15/195	–

The radiological examinations used for the diagnosis of bile leak after surgery were reported as follows: Computed Tomography (CT) was performed in 51 patients, Magnetic Cholangiopancreatography (MRCP) alone in two patients. In two cases, both CT and MRCP were performed.[9,10] Postoperative Percutaneous Transhepatic Cholangiography (PTC) was conducted in only one patient[11] in our database. We identified 81 patients with a surgical drain placed in Morrison space during surgery; in 75 of these patients, a diagnosis of bile leak was made because of bile discharge from the tube.

Treatment of bile leak was described in a total of 180 cases on 195 patients.

Only 19 patients have no clinical deterioration. In this cases, a conservative management was adopted (10.5%). In these cases, the surgical drain was removed when bile leakage stopped. In case of undrained bilioma or free fluid identification, ultrasound or TC-guided percutaneous drainage was positioned in 14 patients to drain the bile outside from the abdominal cavity (7.7%). In one patient, the drainage positioning was the only procedure performed with clinical success (7.1%), in the other cases, it was associated with endoscopic or surgical procedures.

Endoscopic Retrograde Cholangiopancreatography (ERCP) with or without stenting was performed in 155 patients. Data extracted from our database demonstrated that 123 patients (79.3%) achieved clinical success with endoscopic procedures, without any need for further invasive procedures. For ERCP cases failed, surgery was the

Table 2
Patients with intraoperative subvesical duct leak (group 2).
CT, Computed Tomography; MRCP, Magnetic resonance cholangiopancreatography; PTC, Percutaneous Transhepatic Cholangiography; FC, Fluorescent Cholangiography; IOC, Intraoperative Cholangiography.

Group 2	N/Case reported (%)	Successful rate (%)
Pre and intra-operative diagnosis		
• CT	1/36 (2,8)	–
• MRCP	2/36 (2,8)	–
• CT + MRCP	1/36 (2,8)	–
• MRCP + FC	1/36 (2,8)	–
• CT + FC	1/36 (2,8)	–
• CT + MRCP + FC	1/36 (2,8)	–
• IOC	3/36 (8,3)	–
• Direct visualization	26/36 (72)	–
Intra-operative management		
• Clip	16/30 (53,3)	16/16 (100)
• Suture	14/30 (46,7)	14/14 (100)
• Nothing	6/36	2/6 (33,3)

choice with a complete resolution of the complication.

Surgical management was adopted in 37 patients (20.5%) and in 25 patients a re-laparoscopy procedure was performed. In 17 cases (9.4%) surgery was choosen as first-line treatment.

In 15 cases, treatment wasn't described in the text. None of the patients died.

The hospital length of stay (LOS) ranged from 3 to 15 days (median 9).

In group 2, we included total of 36 patients without post-operative SVBD leak operated of LC. Data extracted focused on the preoperative study of biliary tree anatomy and the intraoperative management of detected SVBD (Table 2).

Identification of an aberrant bile duct was done through the support of diagnostic imaging in a total of 7 patients; Preoperative CT scan alone was performed in three patients, preoperative MRCP alone in other three patients and both exams were conducted in one case[18]; in three of these cases Fluorescent Cholangiography (FC) was added during surgery to confirm the presence of an aberrant subvesical duct radiologically identified in the preoperative study.[12–14] Intraoperative diagnosis of SVBD was done through Rx Intraoperative Cholangiography (IOC) in three patients.

In 26 patients, SVBD was directly visualized during surgery diagnosed without the support of any radiological examinations. Identification of undamaged duct during the gallbladder dissection occurred in 6 patients: in all of them, the suture of the duct was deemed unnecessary by the surgeon. In the other 20, SVBD was detected intraoperatively because of bile leak evidence: the injury was managed immediately with ligation or clip positioning and none of these patients presented bile leak in the postoperative period.

In a total of 30 patients included in Group 2, SVBD was closed during surgery, with clip positioning in 53.3% of cases or with laparoscopic suturing in the other 46.7%.

4. Discussion

SVBD are small bile ducts measuring 1–2 mm in diameter usually connected with the right hepatic lobe, close to the gallbladder fossa. They commonly drain into the right hepatic or common bile duct and, less frequently, into the left hepatic duct. They usually don't drain a liver parenchymal portion into the gallbladder.

There isn't a universal classification of Subvesical bile ducts. In the Literature, numerous confusing and contradicting descriptions have been reported, such as accessory, subvesical, subvesicular, supravesicular biliary ducts, or vasa aberrantia.

SVBDs are also incorrectly known as "Ducts of Luschka", from the first definition of "slender bile ducts running along the gallbladder fossa" described by Hubert von Luschka in his textbook of clinical anatomy published between 1862 and 1867.[15]

In particular, Luschka described two different types of ducts associated with the wall of the gallbladder. The first one, later termed "Luschka crypts", referred to intramural glands draining into the gallbladder lumen. The second one consisted of a network

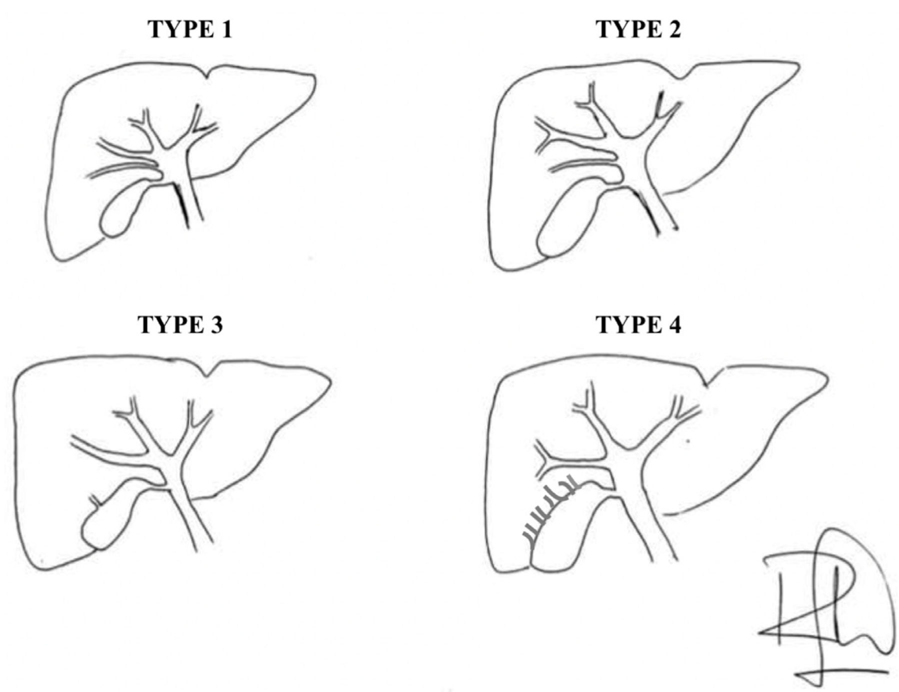

Fig. 2. Types of subvesical bile ducts described by Schnelldorfer. Type 1—segmental or sectorial subvesical bile duct, type 2—accessory subvesical bile duct, type 3— hepaticocholecystic bile duct, type 4—aberrant subvesical bile duct.

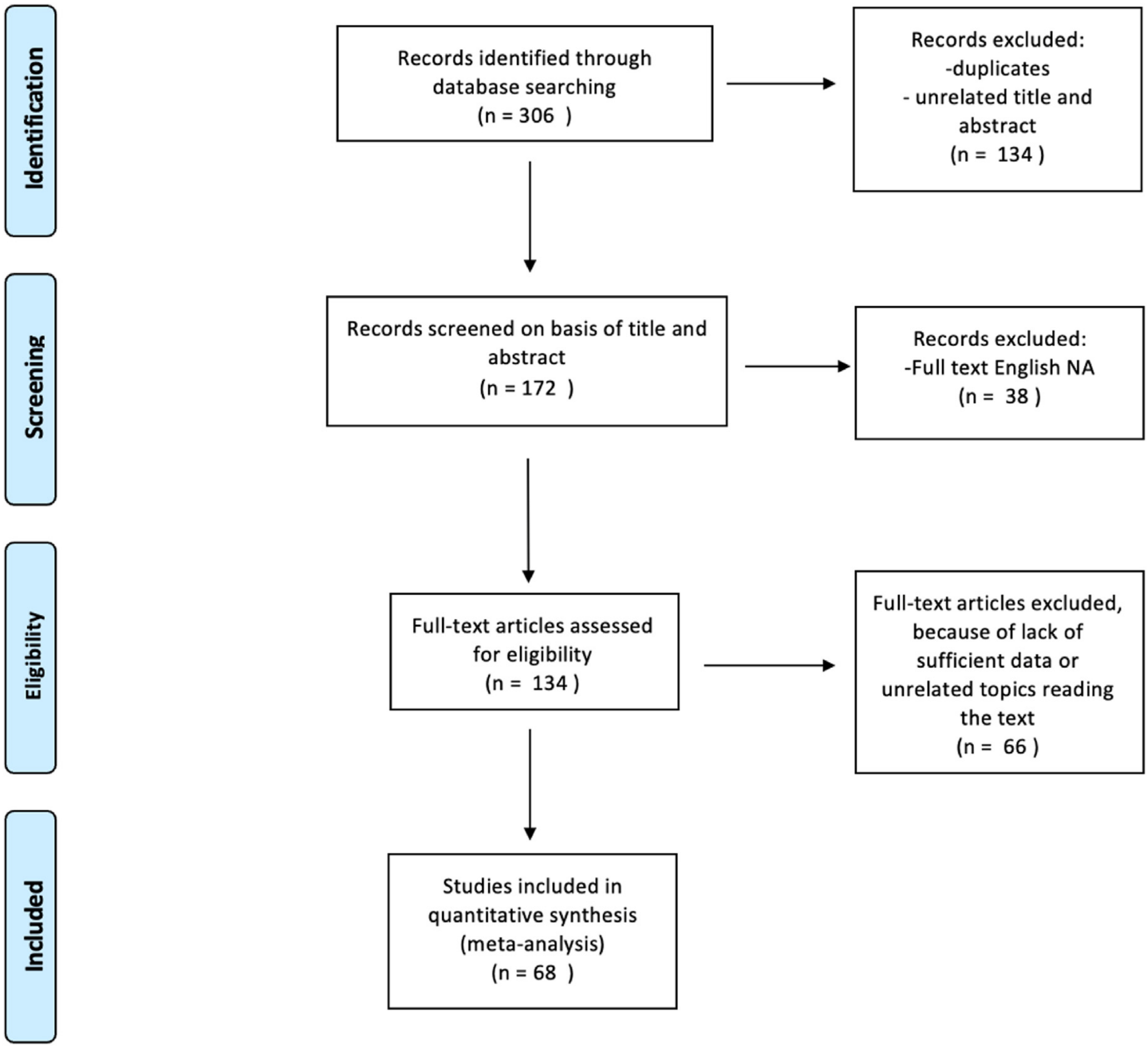

Fig. 3. Selection and inclusion flow diagram.

of microscopic ducts surrounding the gallbladder along his liver bed and the peritoneal surface, like lymphatic vessels.

In 2012, Schnelldorfer[16] explained how over the years, aberrant bile ducts were termed "ducts of Luschka", disagreeing with Luschka's original publication. For this reason, the term "ducts of Luschka" should be replaced by "Subvesical bile duct".

He proposed a definition of "subvesical bile duct" including "any bile duct traversing in close contact with the gallbladder fossa". This description identifies four different types of bile ducts illustrated in Fig. 2.

The prevalence of BDI after LC ranges from 0.3 to 2%[17,18] of cases, higher than after open cholecystectomy. Over the years, many methods have been employed to improve safety during LC, reducing this incidence to 0.08% in a recent study conducted on 156315 patients.[19]

The unsuccessful clipping of the cystic duct stump is the first cause of minor bile leaks after LC.[20] SVBD injury represents the 2nd one, reported up to 0.15% of cases in a large series of 1352 patients.[6,21] The real prevalence of subvesical ducts is challenging to estimate in the general population. Ko et al.[22] reported the incidence of ducts of Luschka as 4.6% in a study conducted on resected liver specimens. Kitami et al.[23] described an incidence of 10% based on preoperative Drip-Infusion Cholangiography-Computed Tomography (DIC-CT) imaging of 277 patients with cholelithiasis. In a study conduct on human fetuses, the incidence of ducts of Luschka was found to be 21.9%.[24] In his review, Schnelldorfer[9] establishes a prevalence of SVBD from 4% to 10% in the general population. However, this data is probably underestimated because of the limited sensitivity of detecting these small ducts.

Preoperative study of the biliary tree anatomy and identification of its variants may be useful to detect thin ducts and avoid inadvertent injury during hepatobiliary surgery.

We found most of studies of European or American group, and a little part of studies are from China, Japan or Korea. In our review, the identification of SVBD before surgery was made through CT, MRCP, or both in a total of 8 patients and the awareness of the presence of SVBD before the gallbladder dissection from its fossa allowed to avoid injury during surgery in 87.5% (7/8) of patients.

5. Intraoperative SVBD leaks management

The anatomic variation could be also detected intraoperatively through contrast media injection into a bile duct. Intraoperative Cholangiography (IOC) is widely used during LC in patients suspected of having bile duct stones, but there is still no consensus of its routine use.[25] Recently, an innovative technique was introduced

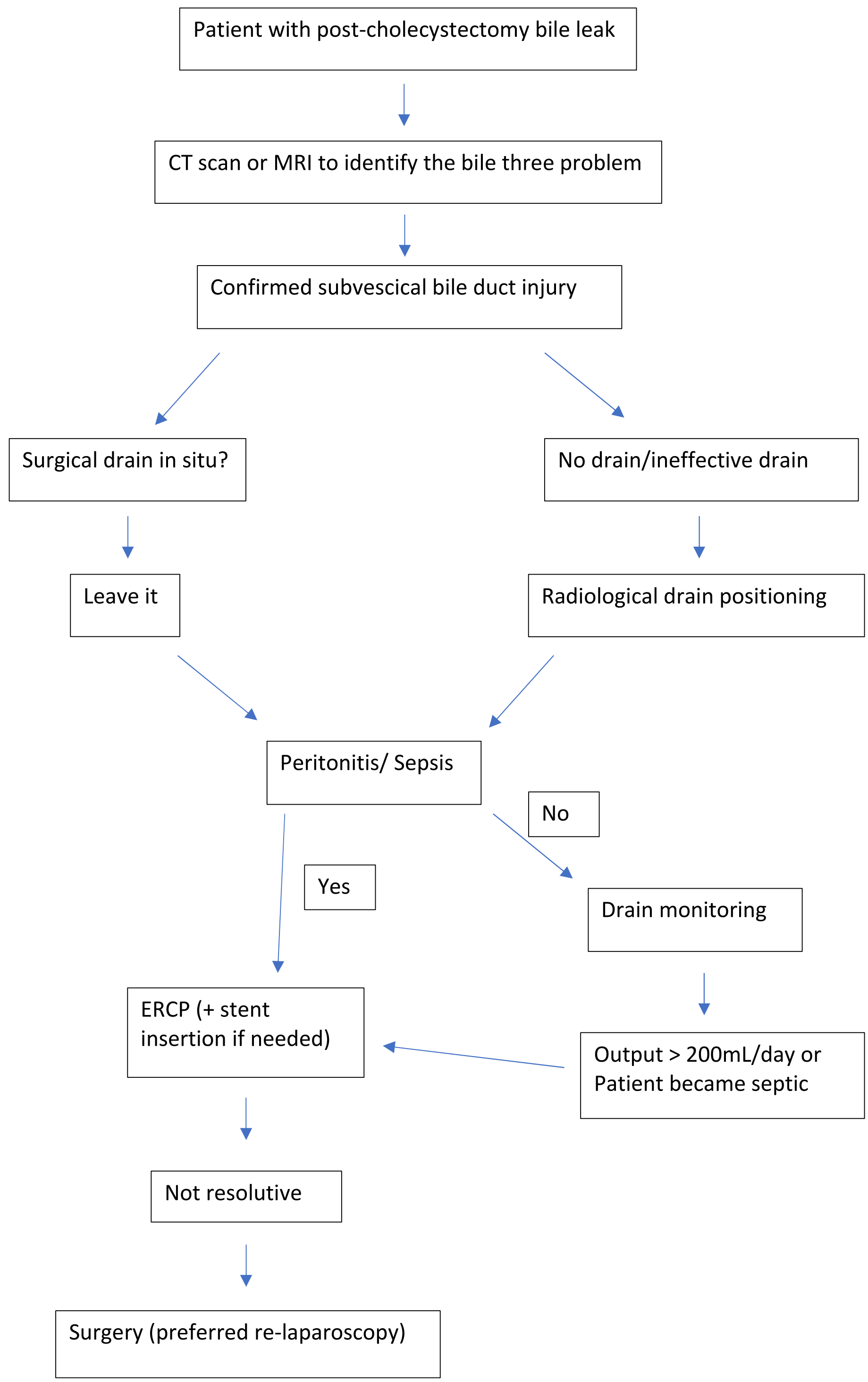

Fig. 4. Protocol recommendation on the management of SVBD injury.

to visualize the map of the biliary tree and detect aberrant biliary ducts: Fluorescent Cholangiography (FC) by intravenous injection of Indocyanine Green (ICG) 2 h before surgery.[26,27] In our review, FC was performed in three cases included in Group 2.

Several causes may play a role in the incidence of leaks from SVBD, such as tissue inflammation, poor visibility of the surgical field, surgical expertise, and an incorrect dissection plane.

A careful examination of the cystic bed after cholecystectomy would help to recognize leaks from an SVBD. When SVBD leak is detected intraoperatively, immediate repair is recommended to manage this complication. Many authors in this review suggest ligating the visible bile duct with a clip[28–31]; other authors chose laparoscopic suture with 3-0 polyglactin (Vicryl) with success.[32,33] Diatermocoagulation of the bile duct is not effective in stopping the bile spill and could worsen the parenchymal damage; therefore it should be avoided. Data extracted from studies included in the review, demonstrated that ligation or clip positioning of SVBD during surgery was performed in a total of 30 patients. In Table 2, out of the six cases of successfully identified SVBD during surgery, surgeons elected not to do anything. However, the success rate for this approach is only 2/6 (33%). This finding suggest that, when surgeon identify a SVBD, an interventiational approach, with ligation or clip positiong, should be the choice.

6. Postoperative SVBD leaks management

When SVBD injury is not recognized intraoperatively, symptomatic minor bile leak is usually diagnosed during the first week after surgery.

The clinical presentation of bile leak changes depending on the amount of bile extravasated, the presence of infected bile, and the positioning of a drain in Morrison's space after surgery. The volume of extravasated bile depends on the caliber of the damaged duct. Usually, bile leak from the subvesical ducts has a small amount and often resolves spontaneously without any treatment, thanks to the abdominal peritoneum's capacity to absorb bile. Therefore, the real incidence of such a condition is unavailable as the asymptomatic occurrence is unknown. However, when the damaged duct is larger and connected with the central biliary tree, the extravasated bile volume may be high. It may lead to severe deterioration in the patient's condition, progressing to bile peritonitis and sepsis.

Endoscopic management is considered the gold standard treatment in case of a minor bile leak. Sphincterotomy and biliary stent placement reduce the transpapillary pressure gradient through the sphincter of Oddi between the biliary tract and the duodenum, favoring drainage of bile into the gastrointestinal tract. Low pressure on the leakage site promotes the healing and closure of the defect, with a clinical success rate reported in the up to 90%.[34] Chandra et al. described 23 patients with bile leak from the duct of Luschka treated with endoscopic procedures with a success rate of 100% of cases; only 5 patients required stent positioning. In his study, endoscopic biliary sphincterotomy alone without stenting is considered the fastest method to manage the bile leak with good outcomes. In fact, stent placement requires a second endoscopy for stent removal. Whereas, Keffles et al.[35] in a study on 100 patients, supported that the optimal intervention for post-cholecystectomy bile leak should include temporary insertion of a biliary stent. Shanda et al.[36] proposed sphincterotomy alone for patients with a low-grade leak and stent placement in patients with a high-grade leak.

If ERCP is not possible or fails, the Percutaneous Transhepatic Drainage (PTCD) is the alternative approach.[17] This radiological intervention consists of the bile diversion away from the site of ductal injury to promote fast healing.

In our review, 124 patients (79.5%) achieved clinical success with endoscopic or radiological procedures, without any need for further surgical procedures.

Surgery approach is controversial. Some authors[37,38] consider re-laparoscopy an effective procedure in managing minor bile leakage after LC and used surgery as the first-line treatment in selected healthy patients without jaundice. Laparoscopic aspiration of leaked bile and lavage of the abdominal cavity are more effective than percutaneous drainage, accelerating patient healing with a shorter hospital stay. We summerized our findings in a protocol recommendation on the management of SVBD injury (Fig. 4).

Our systematic review has several limitations. We found studies with small patient numbers and the evidence comes from mainly retrospective case series or case reports.

7. Conclusions

The incidence of subvesical bile duct leak is not known, and most cases are recognized with intraoperative findings or post-operative bile leak. Our review showed that the best treatment for subvesical duct diagnosed intraoperatively is the immediately ligation or clip positionig. However, for subvesical duct discovered postoperatively, ERCP is the treatment of choice and allows good outcomes, also without stent positioning.

Ethics approval and consent to partecipate

Not applicable.

Consent for publication

Not applicable.

Availability of data and materials

All data generated or analysed during this study are included in this published article and its supplementary information files.

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Authors' contributions

FC, ME and GTC contributions to study conception and design, data analysis and interpretation, and preparation of the manuscript. GM, FD and VM participated in data collection and analysis. MC proofread and revised the manuscript. All authors read and approved the final manuscript.

Declaration of competing interest

The authors declare that they have no competing interests.

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Abbreviations

LC =	Laparoscopic Cholecystectomy
BDIs =	Iatrogenic bile duct injuries
SVBD =	Subvesical bile duct
CHD =	Cholecystohepatic duct
US =	ultrasound
CT =	Computed Tomography
DIC-TC =	Drip Infusion Cholangiography with Computed Tomography
MRI =	Magnetic resonance Imaging
MRCP =	Magnetic resonance cholangiopancreatography
PTC =	Percutaneous Transhepatic Cholangiography
PTCD =	Percutaneous Transhepatic Drainage
IOC =	Intraoperative Cholangiography
FC =	Fluorescent Cholangiography
ICG =	Indocyanine Green
ERCP =	Endoscopic Retrograde CholangioPancreatography

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