Posthepatectomy Bile Leakage

F Sukhum Kobdej

Posthepatectomy Bile Leakage

- Major cause of postoperative morbidity
  - prolonged hospital stay, delayed removal of abdominal drains, and need for additional (invasive) diagnostic tests and interventions
- Abdominal sepsis in severe cases -> death
- May also affect the long term outcome of patients adversely undergoing operative treatment for malignant disease
- The incidence
  - Liver resection without biliary reconstruction ranges from 3.6% to 12%
  - Hepaticojejunostomy ranges from 0.4% to 8%.

M Koch, et al. Surgery 2011;149:680-8

Posthepatectomy Bile Leakage

- Definition, ISGLS
  - Discharge of fluid with an increased bilirubin concentration via the intra-abdominal drains on or after postoperative day 3
  - Or as the need for radiologic intervention (ie, interventional drainage) and relaparatomy for biliary collections and bile peritonitis
  - Increased bilirubin concentration : at least 3 times the serum bilirubin concentration measured at the same time

M Koch, et al. Surgery 2011;149:680-8

Grade A

- Little or no impact on patients' clinical management
- Good clinical condition, and leakage is controlled adequately by an intra-abdominal drain
- Volume of drain fluid usually decreases daily as does the bilirubin concentration of the fluid
- Imaging may show perihepatic fluid collections -> not associated with clinical symptoms
- Prolonged drainage via the intra-abdominal drains (<1 week) may be required and hereby cause a prolonged hospital stay

M Koch, et al. Surgery 2011;149:680-8

Grade B

- Require a change in patients' clinical management but can be treated without relaparotomy
- Compromised clinical condition moderately
  - Parameters suggestive of infection, such as fever and/or abdominal discomfort
- Drains may not entirely drain the leakage -> Imaging studies often are performed
  - Typically demonstrate an intra-abdominal fluid collection and anastomotic leakage (if a bilioenteric anastomosis was performed)
- Require antibiotic therapy, subsequent radiologic and endoscopic procedures are often indicated to control bile leakage
  - Percutaneous intra-abdominal drainage of fluid collections
  - Endoscopic retrograde cholangiography with placement of an intrahepatic stent
  - Percutaneous transhepatic cholangiodrainage
- Prolonged postoperative hospital stay, some patients may be discharged with drains
- Grade A bile leakage requiring drainage for more than 1 week-> Grade B

M Koch, et al. Surgery 2011;149:680-8

Grade C

- Require relaparotomy to control this complication
- Operative procedures include maneuvers such as suture closure of leaking bile ducts, clearance of intraabdominal fluid collections, and (re-)construction of a bilioenteric anastomosis
- Radiologic and/or endoscopic interventions may have been already performed
- May present in a life-threatening condition with severe abdominal pain or bile peritonitis
  - Single or multiorgan failure
  - Often require treatment in a critical care facility
- Radiologic imaging is performed -> signs of either an intra-abdominal fluid collection or an anastomotic leakage (in case of hepaticoenterostomy)
- Prolonged postoperative course and secondary postoperative complications (eg, abdominal wound infection)
- Early postoperative bile leakage after hepaticoenterostomy may represent a special indication for immediate operative intervention and reconstruction of the bilioenteric anastomosis
  - Even though the clinical condition of these patients might be less severe, they also should be classified as having Grade C bile leakage because of the invasiveness of required therapy

M Koch, et al. Surgery 2011;149:680-8

Definition and Grading

Table II. Consensus proposal of the ISGLS for a definition and grading of bile leakage after hepatobiliary and pancreatic surgery

Definition	Bile leakage is defined as fluid with an increased bilirubin concentration in the abdominal drain or in the intra-abdominal fluid on or after postoperative day 3, or as the need for radiologic intervention (ie, interventional drainage) because of biliary collections or relaparotomy resulting from bile peritonitis. Increased bilirubin concentration in the drain or intra-abdominal fluid is defined as a bilirubin concentration at least 3 times greater than the serum bilirubin concentration measured at the same time.
Grade	
A	Bile leakage requiring no or little change in patients' clinical management
B	Bile leakage requiring a change in patients clinical management (eg, additional diagnostic or interventional procedures) but manageable without relaparotomy, *or* a Grade A bile leakage lasting for >1 week
C	Bile leakage requiring relaparotomy

M Koch, et al. Surgery 2011;149:680-8

Risk Factors of Posthepatectomy Bile Leakage

- Exposure of Glisson's sheath on the cut surface (caudate lobectomy, central bisectionectomy, and right anterior sectionectomy)
- Resection of segment 4
- Cut surface area > 57.5 cm^2
- Repeated hepatectomy
- Intraoperative blood loss > 775 ml
- Intraoperative bile leakage
- Prolonged operative time > 300 min
- Peripheral cholangiocarcinoma
- Preoperative chemoembolization.

Hoekstra et al. Dig Surg 2012;29:48–53

Prevention of Bile Leakage

- Meticulously identify any leaking ducts during and after transection and carefully ligate them
- Post-transection testing of potential leaks
  - Injecting saline, methylene blue, indigocarmine, or ICG at cystic duct to identify any bile leaks from the cut surface or hilar plate which -> if found, should be sutured
  - White test : injection of fatty emulsion to biliary tree to detect leakage
  - Cystic duct tube(C-tube) insertion : insert at tube via cystic duct as alternative to T-tube in biliary surgery for biliary decompression -> usefulness could not be confirmed
- Fibrin glue or sealants may be beneficial in decreasing bile leaks

S. Kapoor and S. Nundy. HPB Surgery · May 2012
Linke R, et al.Annal of Hepatology , 2015; 14 (2): 161-167
A. Nanashima et al. HPB(Oxford) 2012 Nov 19;15(7):517–522

Management

- Early bile leaks
  - Bile stained drain effluent
  - Undrained leaks usually result in increasing abdominal pain and a low-grade fever, later progressing to sepsis
- Generalized biliary peritonitis requires laparotomy or laparoscopy for lavage and drainage
- Localized collections can usually be drained percutaneously
- Most bile leaks will settle spontaneously
  - A drain output of >100 ml on the tenth postoperative day is associated with a failure of conservative management
  - Some report recommended ERCP in high-output bile leak beyond 1 wk or persistent low output beyond 3 wks (low output :< 300 ml/day, high output :> 300 ml/day)
  - Persistent fistulae despite ERCP and stenting or nasobiliary drainage require relaparotomy and enteric drainage

C. Walsh and A. Ben Creswell. Surgery,2022
S. Kapoor and S. Nundy. HPB Surgery · May 2012

Classification

- Nagano et al. proposed classification of posthepatectomy bile leakage according to the postoperative fistulogram and biliary scintigram
  - Type A, minor leakage, with only a small amount of bile leakage or an amount that decreased daily
  - Type B, major leakage due to insufficient closure of the bile duct stump
  - Type C, major leakage due to injury of the bile duct
  - Type D, division of the bile duct

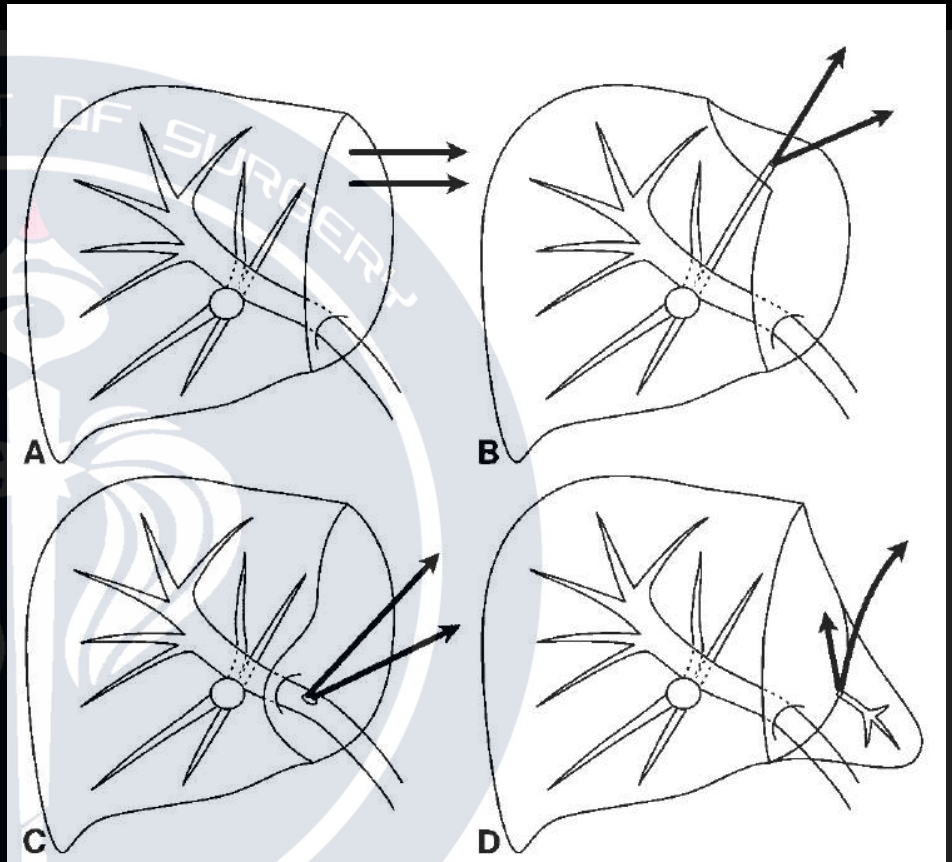

Fig. 1. Patients with postoperative bile leakage were classified into the following four groups: type A, minor leakage, with only a small amount of bile leakage; type B, major leakage due to insufficient closure of the bile duct stump; type C, major leakage due to injury of the bile duct; type D, major leakage due to division of the bile duct.

Nagano et al.: Bile Leakage after Hepatic Resection. World J. Surg. Vol. 27, No. 6, June 2003

Management

- Proximal bile ducts (types B and C) took longer to heal than those without bile duct involvement (type A) (102.6 vs. 37.8 days)
- Peripheral bile duct (type D) suffered from uncontrollable leakage and required reoperation
- Biliary drainage -> shorter healing times (30 vs. 179 days), supporting the conclusion that biliary drainage is useful
- Nasobiliary tubes
  - Early fluoroscopic detection of the status of leakage, easy removal without repeated endoscopy, and preservation of papillary function

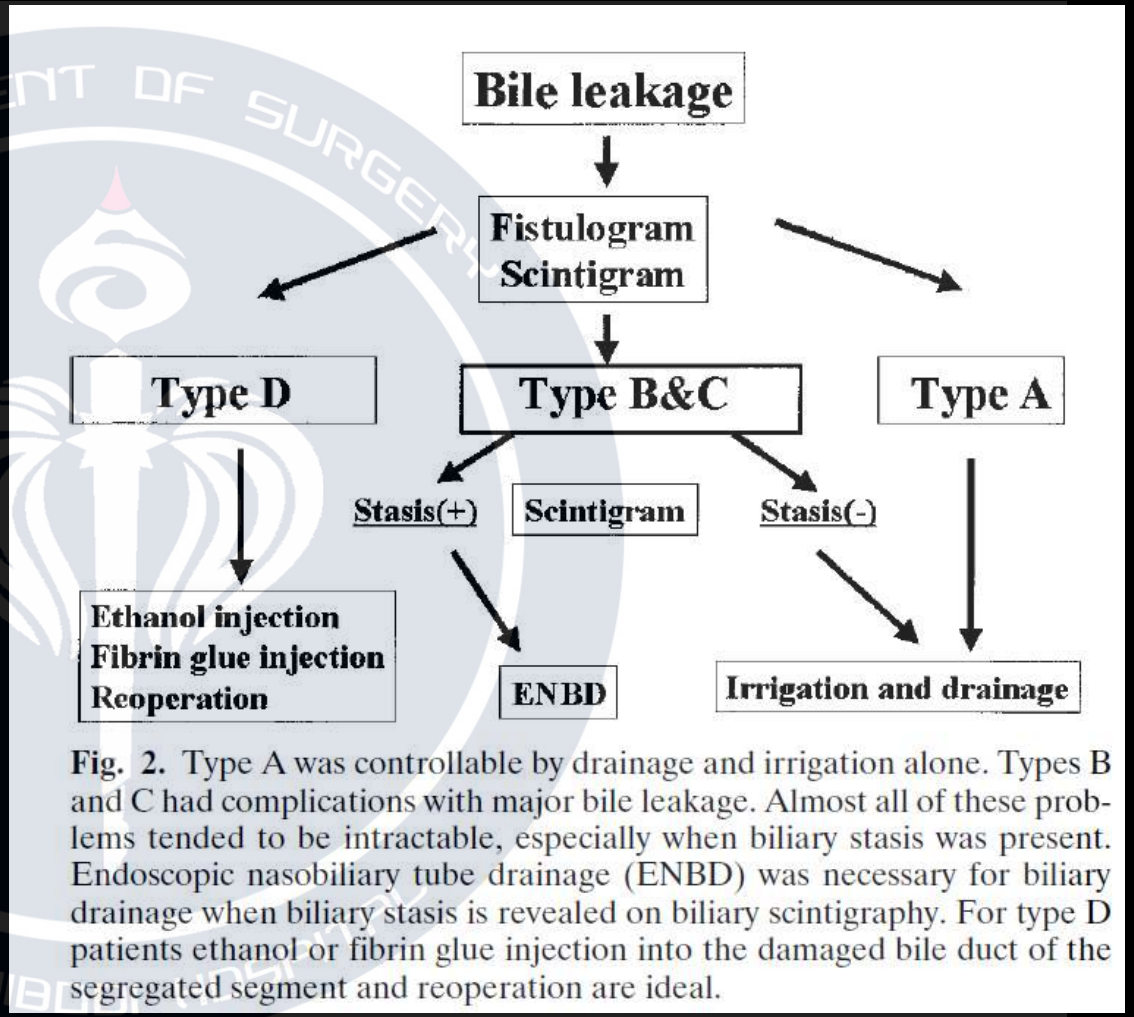

Fig. 2. Type A was controllable by drainage and irrigation alone. Types B and C had complications with major bile leakage. Almost all of these problems tended to be intractable, especially when biliary stasis was present. Endoscopic nasobiliary tube drainage (ENBD) was necessary for biliary drainage when biliary stasis is revealed on biliary scintigraphy. For type D patients ethanol or fibrin glue injection into the damaged bile duct of the segregated segment and reoperation are ideal.

Nagano et al.: Bile Leakage after Hepatic Resection. World J. Surg. Vol. 27, No. 6, June 2003

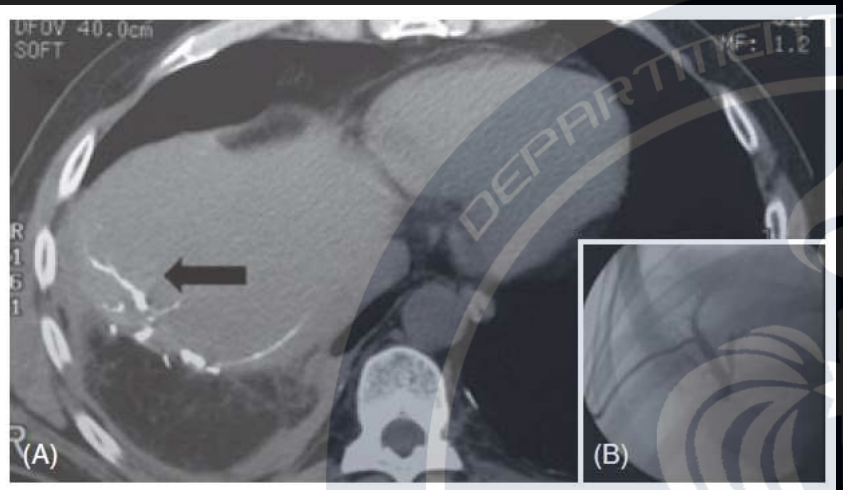

Figure 2 (A) Plain computed tomography performed after percutaneous cholangiography shows a communicating biliary fistula adjacent to the resected surface of the liver (black arrow). (B) Percutaneous cholangiography demonstrating no communication between a dilated intrahepatic bile duct and the principal bile duct

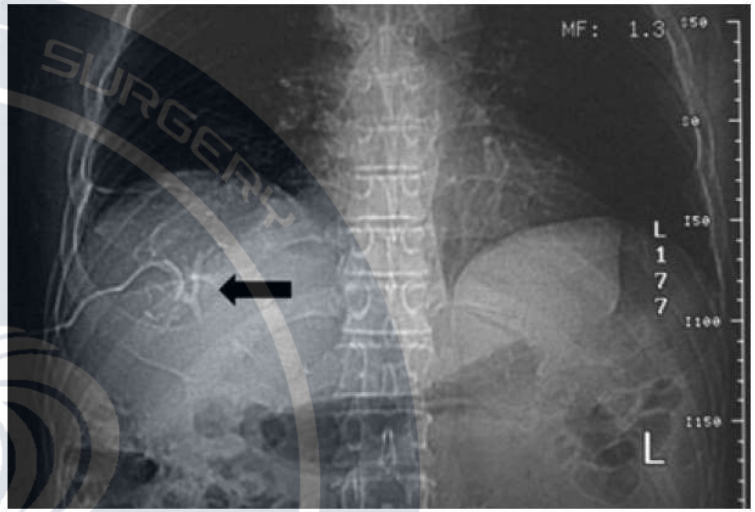

Figure 3 Demonstration of the right anterior branch of the biliary system by fistulography. A distal injury to the bile duct was responsible for the non-communicant biliary fistula. The bile duct which was ligated proximally during the initial hepatectomy was mistakenly preserved as part of the anterior segment of the right liver

C Honore et al. HPB 2009, 11, 364–369

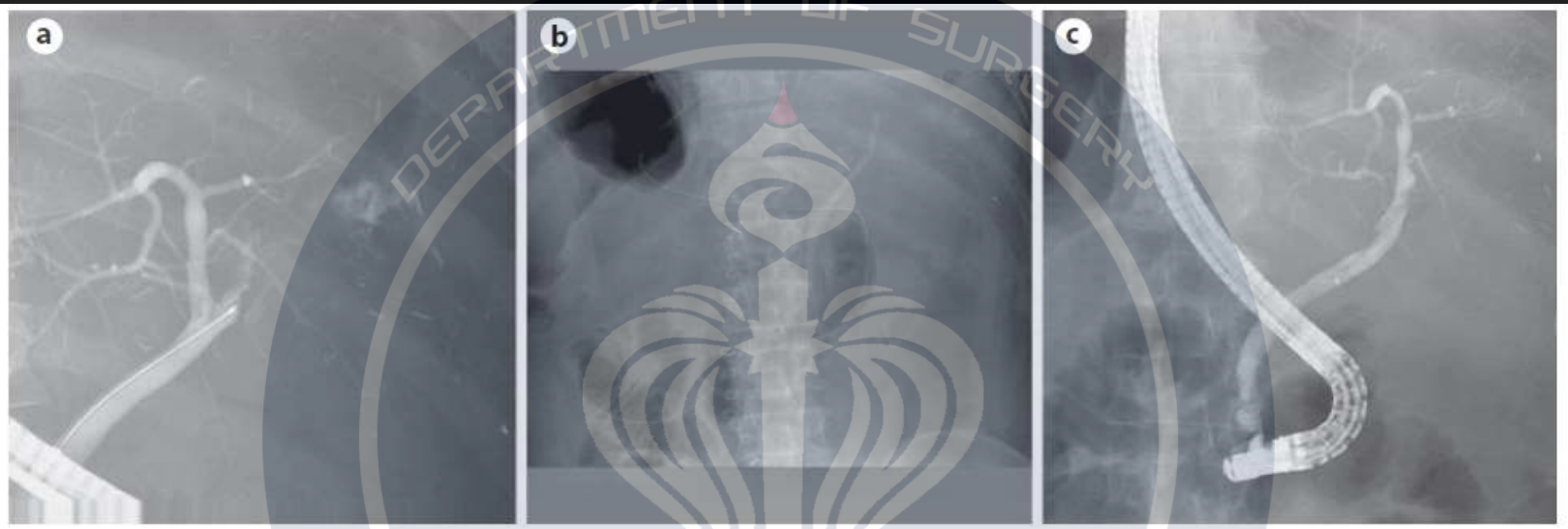

Fig. 1. a Endoscopic retrograde cholangiopancreaticography showing biliary leakage of the stump of the right hepatic duct after right hemihepatectomy. **b** ERCP with stent placement. **c** Six weeks later, bile leakage subsided.

Hoekstra et al. Dig Surg 2012;29:48–53

Isolated Bile Leakage

- Type D bile leakage, incidence 0.1-1%
- Not improve after drainage procedure, usually require other procedures
- Risk factor
  - Bile duct anomalies
  - Rt hepatectomy -> bile leak from bile duct of segment 1
  - Lt hepatectomy -> damaged Rt posterior bile duct draining to Lt duct
- Prevention
  - Preoperative biliary tree images and perioperative assessment
  - Intraoperative cholangiogram; through cystic duct before bile duct ligation
  - Anatomical resection

KUBO and SHIRABE.*Ann Gastroenterol Surg.* 2020;4:47–55.

Isolated Bile Leakage

- Surgical treatment
  - Timing of surgical intervention was based on non-responsiveness to external drainage and/or the persistence of intra-abdominal sepsis
    - Mostly several months after the first operation
  - A planned approach was based on the patient's general status, volume of future liver remnant and liver functional reserve, type and extent of injury, and volume of the causing IBL
  - Some report suggested early reoperation before development of intraabdominal sepsis -> difficult to determine whether IBL can be managed by non-surgical treatment

KUBO and SHIRABE.*Ann Gastroenterol Surg.* 2020;4:47–55.

Isolated Bile Leakage

- Surgical treatment
  - Type of surgical treatment
    - Estimated volume of the liver remnant
    - Functional reserve of the liver
    - Intraoperative factors, such as adhesions, infection, abscess formation
    - Anatomical distortions caused by regeneration of the remaining liver
    - Anatomical errors of the first operation
  - Liver resection of the independent liver parenchyma containing the fistula
  - Bilioenteric anastomosis
    - A percutaneous transhepatic drain at excluded bile duct before operation for guiding hilar plate dissection and facilitating the location of the excluded duct
    - Anastomosis between the jejunum and the fistula was created using the drainage catheter as a guide
    - Risk for severe cholangitis and liver abscess after the operation in poor bile flow

KUBO and SHIRABE.*Ann Gastroenterol Surg.* 2020;4:47–55.

TABLE 2 Surgical treatment for isolated bile leakage

Author	Reported year	Rate of isolated bile leakage	Diagnosis	First operation	Independent liver segment	Non-surgical treatment before 2nd operation	Period between 1st and 2nd operations	Second operation	Operating time (min)	Blood loss (mL)	Postoperative hospital stay (d)	Complication
Fukuhisa et al[15]	2017	ND	HCC	Right hepatectomy	S1	Percutaneous drainage	48 d	Resection of S1	ND	ND	15	No
Fragulidis et al[13]	2008	3/234 (1%)	CCC	Right extended hepatectomy	S1	Percutaneous drainage	6 m	Resection of S1	ND	ND	ND	Uneventful
			Hydatid cyst	Resection of segment 5	Posterior	Percutaneous drainage	8 m	Resection of S6 and S7	ND	ND	ND	Uneventful
			Hydatid cyst	Left lateral sectionectomy	S4, Posterior	Percutaneous drainage	14 m	Resection of S4 and biliary-enteric anastomosis	ND	ND	ND	Uneventful
Honore et al[10]	2009	3/2409 (0.1%)	Hepatic abscess after laparoscopic cholecystectomy	Right hepatectomy	Remnant S 5/8	Percutaneous drainage	18 m	Resection of S5/8 and hepaticojejunostomy	401	450	30	Fistula on the bilio-digestive anastomosis
			HCC	Right hepatectomy	Remnant S 5/8	Percutaneous drainage	3 m	Resection of S5/8	310	2020	10	Uneventful
			HCC	Right hepatectomy	S6	PTPE, TAE and direct closure	12 m	Resection of S6	405	2300	13	Uneventful
Patrono et al[11]	2014	–	Hepatic injury	Left hepatectomy	S6/7	ENBD PTCD	Early timing	Bilioenteric anastomosis	ND	ND	ND	Uneventful
			Donor of LDLT	Right trisectionectomy	S2	PTCD	5 months	Bilioenteric anastomosis	ND	ND	ND	Uneventful
Hoekstra et al[12]	2012	1/315 (0.3%)	Focal nodular hyperplasia	Right hepatectomy	Left segmental bile duct	–	–	Bilioenteric anastomosis	ND	ND	ND	Bile leakage
Sakamoto et al[27]	2016	2/334 (0.6%)	–	Right anterior sectionectomy	Posterior	Percutaneous drainage and PTPE	–	Fistulojejunostomy	ND	ND	323	ND

Abbreviations: CCC, cholangiocellular carcinoma; d, days; ENBD, endoscopic nasobiliary drainage; HCC, hepatocellular carcinoma; LDLT, living-donor liver transplantation; m, months; ND, not described; PTCD, percutaneous transhepatic cholangio-drainage; PTPE, percutaneous transhepatic portal vein embolization; S, segment; TAE, transcatheter arterial embolization.

KUBO and SHIRABE.*Ann Gastroenterol Surg.* 2020;4:47–55.

Isolated Bile Leakage

- Non-surgical treatment
  - Endoscopic treatment
    - Endoscopic drainage to the common bile duct is ineffective for IBL
    - Some report of bridging stent treatment
      - Transpapillary stent -> the peritoneal cavity to drain the associated bilious collection
      - Second stent -> bile duct to ensure proper biliary drainage for the rest of the liver
    - Fluoroscopy-guided transgastric hepaticoantrostomy
    - The rendezvous procedure, which combines endoscopic techniques with percutaneous techniques to continue the biliary continuity
    - Minimally invasive procedures and cause little damage to liver function
      - Only a few reports of endoscopic treatment because it is not widely carried out

KUBO and SHIRABE.*Ann Gastroenterol Surg.* 2020;4:47–55.

Isolated Bile Leakage

- Non-surgical treatment
  - Bile duct ablation therapy
    - Ethanol was commonly used for bile duct ablation therapy; acetic acid was used in one case and N-butyl cyanoacrylate in another
    - Selective intrahepatic biliary ethanol injection -> destroyed the biliary epithelium, permeated the parenchyma, induced hepatocyte degeneration, and resulted in compensatory hypertrophy of the non-injective hepatic lobe in an animal study
    - Bile duct ablation therapy -> done for IBL with no communication with the biliary tree because ethanol results in irreversible damage to the remaining bile ducts
      - Confirm that the leaking bile ducts do not communicate with the biliary tree by carrying out fistulography and ERCP
    - Most cases of IBL that were treated with ethanol ablation therapy involved less than one segment
    - When the liver volume is large, or when the amount of leaked bile is high, IBL may often not be cured by ethanol ablation therapy

KUBO and SHIRABE.*Ann Gastroenterol Surg.* 2020;4:47–55.

Isolated Bile Leakage

- Non-surgical treatment
  - Percutaneous transhepatic portal vein embolization
    - Induces atrophy of hepatocytes and decreases the amount of bile duct juice
    - Suitable for IBL from one or more liver segments
    - Used to decrease the amount of bile leakage from a large area of the isolated bile duct when ethanol injection was ineffective
    - Combination therapy with bile duct ablation after PTPE was reported to be useful
    - PTPE should be done only when patients are in good condition, with sufficient remnant liver function to avoid liver failure

KUBO and SHIRABE.*Ann Gastroenterol Surg.* 2020;4:47–55.

Isolated Bile Leakage

- Non-surgical treatment
  - Transcatheter arterial embolization
    - Mentioned in some report
      - TAE in the anterior segmental artery was carried out to stop the production of bile in the injured part of the anterior segment after simple drainage and ethanol injection treatment failed
    - Patients with a liver abscess after TAE are at high risk of developing bile duct infection because of liver parenchyma necrosis after TAE
    - When bile leakage was detected after hepatectomy, almost all cases had abdominal infections
    - TAE may be adaptable only when the bile leakage area is very small; otherwise, infectious complications may arise

KUBO and SHIRABE.*Ann Gastroenterol Surg.* 2020;4:47–55.

Isolated Bile Leakage

- Non-surgical treatment
  - Fibrin glue
    - After confirmation that the fistula was free of infection and that the volume was less than 50 mL/day
      - Fistula was completely sealed with a mixture of fibrin glue and iodized oil -> immediately closed without any major complications
    - Required to have a low volume of bile leakage for treatment with fibrin glue
    - Treatment with fibrin glue was reported in only two cases, and the treatment effect was limited

KUBO and SHIRABE.*Ann Gastroenterol Surg.* 2020;4:47–55.

TABLE 3 Non-surgical treatment for isolated bile leakage

Author	Reported year	Rate of isolated bile leakage	Diagnosis	First operation	Independent liver segment	Treatment method	Outcome
Kyokane et al[30]	2002	ND	Gallbladder carcinoma	Right hepatectomy	S2	Ethanol injection	
Sakaguchi et al[31]	2011	–	Liver metastasis from GIST	Extended left hepatectomy	S5 + 1	Ethanol injection	
Shimizu et al[32]	2006	–	HCC	Right posterior sectionectomy	Anterior bile duct	Ethanol injection	Alive
Matsumoto et al[33]	2002	–	HCC	Right hepatectomy	Caudate lobe	Ethanol injection	Alive
Nakagawa et al[4]	2017	1/631 (0.2%)	–	–	–	Ethanol injection	
Kusano et al[19]	2003	–	Liver abscess with intrahepatic stones	Left hepatectomy	S4	Ethanol injection	Alive
Yamashita et al[8]	2001	3/781 (0.4%)	–	–	–	Ethanol injection with balloon catheter occlusion	
			–	–	–	Ethanol injection	
			–	–	–	Ethanol injection	
Sakamoto et al[27]	2016	2/334 (0.6%)	–	Right anterior sectionectomy	Posterior	Ethanol injection	Alive
Park et al[14]	2005	–	Biliary cystadenocarcinoma	Left extended hepatectomy	Posterior	Acetic acid	Alive
Kim et al[34]	2012	–	HCC	Central bisectionectomy	S8	N-butyl cyanoacrylate	Alive
Kataoka et al[35]	2011	–	HCC	S5 segmentectomy	–	Ethanol injection into the liver parenchyma	Alive
Kubo et al[23]	2018	–	HCC	Partial hepatectomy of S4/5	S5 + 8	Combination therapy with ethanol injection and PTPE	Alive
Sadakari et al[36]	2008	–	Liver metastasis from rectal cancer	Central bisectionectomy	Posterior	PTPE	Alive
Hai et al[37]	2012	–	HCC	Right anterior sectionectomy	Posterior	PTPE	Alive
Ikeda et al[38]	2015	–	Gallbladder cancer	Extended cholecystectomy	S5	TAE	
Tanaka et al[39]	2002	2/363 (0.6%)	CCC	Left hepatectomy	Caudate branch	Fibrin glue	Alive
			HCC	Partial hepatectomy	–	Fibrin glue	Alive
Mutignani et al[28]	2017	–	Cholangiocarcinoma	Right hepatectomy	Left lobe branch	Bridging stent	
Lee et al[29]	2015	–	HCC	Left trisectionectomy	Posterior	Fluoroscopy-guided transgastric hepaticoantrostomy	

Abbreviations: CCC, cholangiocellular carcinoma; GIST, gastrointestinal stromal tumor; HCC, hepatocellular carcinoma; PTPE, percutaneous transhepatic portal vein embolization; TAE, transcatheter arterial embolization.

KUBO and SHIRABE.*Ann Gastroenterol Surg.* 2020;4:47–55.

Isolated Bile Leakage

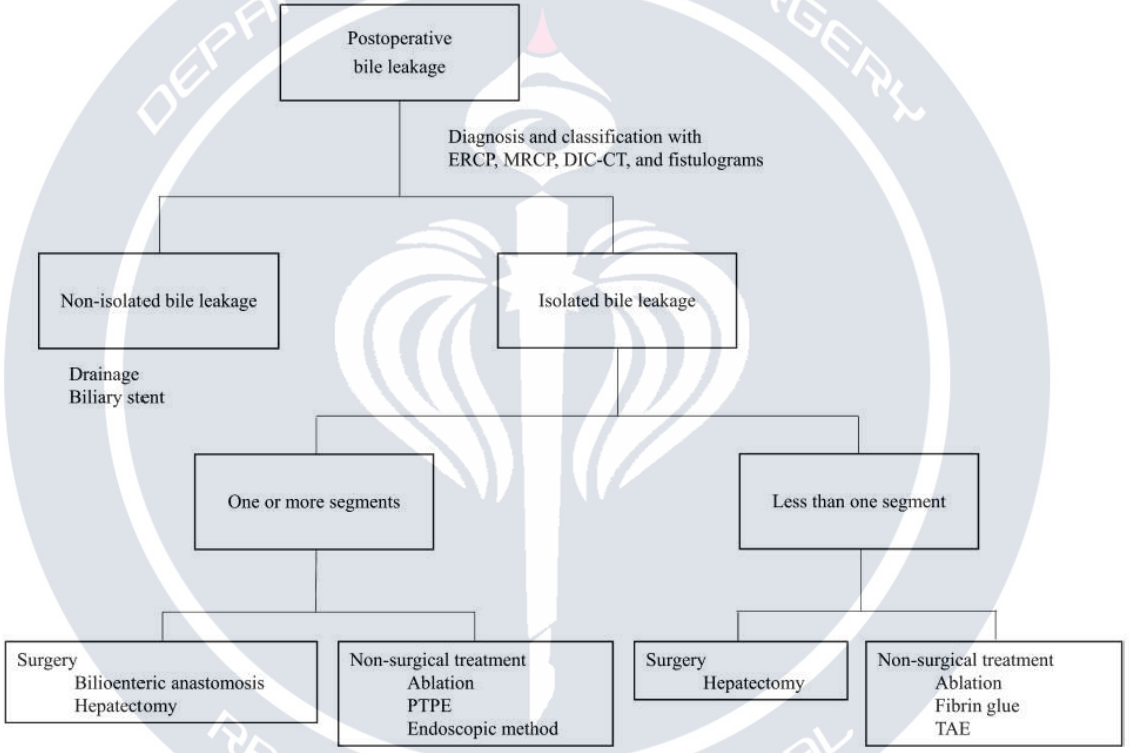

FIGURE 2 Postoperative bile leakage was diagnosed and classified by endoscopic retrograde cholangiopancreatography (ERCP), magnetic resonance cholangiopancreatography (MRCP), drip-infusion cholangiography with computed tomography (DIC-CT), and fistulograms. Therapeutic strategy of isolated bile leakage was classified by the quantity of bile leakage and as either surgical or non-surgical treatment. When the isolated bile leakage was from less than one liver segment, the first choice of treatment method was non-surgical treatment such as ethanol ablation. When the isolated bile leakage was from more than one segment, the first choice of treatment method was surgical treatment. PTPE, percutaneous transhepatic portal vein embolization; TAE, transcatheter arterial embolization

KUBO and SHIRABE. *Ann Gastroenterol Surg.* 2020;4:47–55.

Thank You