ABSTRACT

OBJECTIVE: Bile leakage, while rare, can be a complication seen after cholecystectomy. It may also occur after hepatic or biliary surgical procedures. Etiology may be underlying pathology or surgical complication. Endoscopic retrograde cholangiopancreatography (ERCP) can play major role in diagnosis and treatment of bile leakage. Present study was a retrospective analysis of outcomes of ERCP procedure in patients with bile leakage.

METHODS: Patients who underwent ERCP for bile leakage after surgery between 2008 and 2012 were included in the study. Etiology, clinical and radiological characteristics, and endoscopic treatment outcomes were recorded and analyzed.

RESULTS: Total of 31 patients (10 male, 21 female) were included in the study. ERCP was performed for bile leakage after cholecystectomy in 20 patients, after hydatid cyst operation in 10 patients, and after hepatic resection in 1 patient. Clinical signs and symptoms of bile leakage included abdominal pain, bile drainage from percutaneous drain, peritonitis, jaundice, and bilioma. Twelve (60%) patients were treated with endoscopic sphincterotomy (ES) and nasobiliary drainage (NBD) catheter, 7 patients (35%) were treated with ES and biliary stent (BS), and 1 patient (5%) was treated with ES alone. Treatment efficiency was 100% in bile leakage cases after cholecystectomy. Ten (32%) cases of hydatid cyst surgery had subsequent cystobiliary fistula. Of these patients, 7 were treated with ES and NBD, 2 were treated with ES and BS, and 1 patient (8%) with ES alone. Treatment was successful in 90% of these cases.

CONCLUSION: ERCP is an effective method to diagnose and treat bile leakage. Endoscopic treatment of postoperative bile leakage should be individualized based on etiological and other factors, such as accompanying fistula.

Keywords: Biliary fistula; ERCP; postoperative bile leakage.
Most complications after surgical interventions on biliary system are related to iatrogenic injuries. Biliary injury may result in bile leakage (biliary fistula), bile duct obstruction or bile duct stricture. Bile leakage most commonly occurs after cholecystectomy. Laparoscopic cholecystectomy is more commonly associated with bile injuries than its open counterpart [1, 2]. The incidence of biliary injuries after laparoscopic cholecystectomy varies between 0.5–0.9 percent in different series [3]. Other causes of biliary leakage include orthotropic liver transplantation, hydatid cyst surgery involving the biliary system, liver biopsy, Trans jugular intrahepatic portosystemic shunt (TIPS), hepatic tumor ablation, penetrating sharp object injuries, and blunt object injuries. Irrespective of the nature of injury, the majority of bile injuries cannot be detected during surgery [4]. Surgical therapy of bile leakages at the postoperative period increases patient morbidity and mortality [5, 6]. Endoscopic retrograde cholangiopancreatography (ERCP) plays a major role for treating postoperative bile leakages.

The aim of this study was to analyze the clinical, laboratory, radiological, and endoscopic characteristics of, and the efficiency of endobiliary prosthesis in patients with bile leakage after abdominal surgery who were treated with ERCP in Ankara Numune Training and Research Hospital retrospectively.

**MATERIALS AND METHODS**

This study included a total of 31 patients diagnosed as bile leakage and treated with ERCP after biliary surgery or liver surgery performed for various etiologies in Ankara Numune Training and Research Hospital between January 2008 and May 2012.

Patients' age, sex, etiology for surgical intervention, symptoms, physical examination findings, complete blood counts and blood chemistry results, and daily amount of discharge (ml) from abdominal drain before the endoscopic therapy were recorded. The radiological, endoscopic, and other diagnostic methods used for the detection of bile leakage were evaluated. ERCP was performed by a single experienced endoscopist using side-viewing duodenoscope at a single center. The site and grade of leakage, endoscopic treatment method, the type of injury, and the size of endobiliary prosthesis if used for endoscopic therapy were also recorded.

The severity of bile leak was classified by endoscopic retrograde cholangiography into low grade (leak identified only after intrahepatic opacification) or high grade (leak observed before intrahepatic opacification). Injury type was categorized according to Strasberg's classification. The findings of control cholangiography, and the complications detected during and after endoscopic therapy were recorded.

In patients with postoperative bile leakage after hydatid cyst surgery the preoperative anatomic localization, diameter, and type (Gharbi) of the cyst were recorded.

The endoscopic therapy was considered successful when no signs of bile leakage was observed in the control cholangiography after endoscopy, or when a patient's radiological, clinical, and laboratory findings improved after endoscopic treatment but no control cholangiogram was taken at discharge.

**RESULTS**

The study included a total of 31 subjects (10 males and 21 females). The mean age of the patients were 53.4±13.2 and 50.8±19.5 years for male and female subjects, respectively. The clinical signs or symptoms of bile leakage included abdominal pain in 26 patients (83%), bile drainage from percutaneous drain in 23 (74%) patients, peritonitis in eight (25%) patients, bilioma in three (9%) patients, and jaundice in six (19%) patients. Demographic features, indication for operation, type of operation and signs and symptoms of patients with bile leakage were summarized on Table 1.

The leak was from a cystic stump in 11 (55%) of cases, from right peripheric bile ducts in two (10%),
gall bladder bed in 5 (25%), common hepatic duct in one (5%), and common bile duct in one (5%) after cholecystectomy. Among these patients, 18 (90%) had a Strasberg type A injury and two (10%) had a type D injury. A low-grade leakage was observed in 16 (80%) of the cases and a high-grade leakage in 4 cases (20%) after cholecystectomy.

Twelve (60%) patients with bile leakage were treated by endoscopic sphincterotomy (ES) and nasobiliary drainage (NBD) catheter; seven (35%) by ES and biliary stent (BS); one (5%) by ES alone. Common bile duct stones were detected by ERCP in five (25%) of these patients. All cases with bile leakage after cholecystectomy (n=20) were treated in a single session. The mean duration of follow-up with NBD was 12.4 days (minimum 6, maximum 12 days) in the cases treated by NBD and ES. Bile drainage from bile drain ceased after a mean of 4 days (2–7 days) in 9 cases treated by NBD and ES. There was a low-grade leakage in 9 cases and a high-grade leakage in 3 cases treated by NBD and ES. Eight cases treated by

| Table 1. Demographic features, indication for operation, type of operation and signs and symptoms of patients with bile leakage |
|---------------------------------------------------------------|
| Parameters                               | Total (n=31)           |
|                                            | n     | %    |
| Age (years)                               | 51±17.4 |
| Sex                                       |       |
| Male                                      | 10    | 32   |
| Female                                    | 21    | 68   |
| Type of operation                         |       |
| Laparoscopic cholecystectomy              | 14    | 45   |
| Hydatid cyst surgery                      | 10    | 32   |
| Open cholecystectomy                      | 6     | 19   |
| Hepatic resection                         | 1     | 3    |
| Signs and symptoms associated with bile leakage |       |
| Abdominal pain                            | 26    | 83   |
| Postoperative biliary drainage            | 23    | 74   |
| Peritonitis                               | 8     | 25   |
| Jaundice or hyperbilirubinemia            | 6     | 19   |
| Bilioma                                   | 3     | 9    |

| Table 2. Patients having bile leakage after cholecystectomy |
|-----------------------------------------------------------|
| Injuy type           | Total (n=20) |
|                      | n | % |
| Strasberg type A     | 18 | 90 |
| Strasberg type D     | 2  | 10 |
| Leakage severity     |   |   |
| Low-grade            | 16 | 80 |
| High-grade           | 4  | 20 |
| Applied treatment    |   |   |
| ES+NBD               | 12 | 60 |
| ES+BS                | 7  | 35 |
| ES                   | 1  | 5  |
| Complication         |   |   |
| Minor bleeding       | 4  | 20 |
| Treatment efficiency | 20 | 100 |

BS: Biliary stent; ES: Endoscopic sphincterotomy; NBD: Nasobiliary drainage.

| Table 3. Clinical characteristics, applied treatment, and treatment efficiency in cases with cystobiliary fistula after hydatid cyst surgery |
|-------------------------------------------------------------------------------------------------------------------------------------|
| Preoperative                                                                 | n=10 |
| Overt                                                                   | 1    |
| Occult                                                                  | 9    |
| Postoperative (Bile drainage from drain)                                | 10   |
| Gharbi type                                                            |       |
| Type 2                                                                  | 1    |
| Type 3                                                                  | 8    |
| Type 4                                                                  | 1    |
| Applied Treatment                                                      |       |
| ES                                                                      | 1    |
| ES+NBD                                                                 | 7    |
| ES+BS                                                                   | 2    |
| Treatment efficiency                                                   |       |
| ES+NBD                                                                  | 6/7  |
| ES+BS                                                                   | 1/2  |
| ES                                                                       | 1/1  |

BS: Biliary stent; ES: Endoscopic sphincterotomy; NBD: Nasobiliary drainage.
NBD and ES underwent a control cholangiography and were free of any persistent leakage. All of these cases were successfully treated in a single session. Patients having bile leakage after cholecystectomy are summarized in Table 2.

Two of the cases treated by BS and ES were treated using a 10 Fr plastic stent and 5 patients were treated using a 7 Fr plastic stent. Bile drainage from surgical drain ceased in 2 days (1–3 days) in four of these patients. Cases treated by BS, 6 had low-grade leakage and 1 had high-grade leakage. These cases were successfully treated in a single session. No severe, ERCP-related complications were observed.

One case presenting with postoperative bile drainage from surgical drain following left lobectomy for rectum Ca metastasis was treated by a 10 Fr BS in a second ERCP session upon persistent bile drainage from surgical drain at 11th day after NBD and ES and in the absence of effective bile drainage from NBD.

Ten (32%) of the patients were occurred after hydatid cyst surgery and had cystobiliary fistula. All of these cases presented with bile drainage from surgical drain in the postoperative period, with one having overt cystobiliary communication with signs of preoperative cholangitis and cholestasis. Hydatid cysts were located in right hepatic lobe in 4 cases, hilus or central section in 5 (50%), and left hepatic lobe in 1. According to the Gharbi classification, 8 had type 3, 1 had type 2, and 1 had type 4 hydatid cyst. Only one case had signs suggestive of overt cystobiliary communication on preoperative ultrasound. Seven patients were treated by ES and NBD, 2 by ES and BS, and 1 (8%) by ES alone. Three cases had papillary stenosis on ERCP. Six out of 7 patients treated by ES and NBD had favorable outcomes. One case had failed treatment by NBD and ES and underwent surgery. The mean NBD follow-up was 9 days (3–14 days). One case with postoperative low-output cystobiliary communication was successfully treated by ES alone. One out of two patients treated by BS (7 Fr) and ES was successfully treated while one case was successfully treated by NBD at a second session after failed BS therapy. An overall analysis of cases undergoing endoscopic therapy for cystobiliary fistula after hydatid cyst surgery revealed that 9 (90%) cases were successfully treated by ERCP. No serious, ERCP-related complication was encountered.

**DISCUSSION**

Bile leakage is a rare complication that most commonly occurs after cholecystectomy. Biliary injuries are more common after laparoscopic cholecystectomy than open cholecystectomy [7]. Biliary injury is categorized into major and minor forms, the former involving common bile duct or common hepatic duct while the latter involving common bile duct or common hepatic duct while the latter involving peripheric ducts.

The mechanisms of bile injuries during laparoscopic cholecystectomy have been well defined [8, 9]. The most common scenario involves inadvertently injuring common bile duct by confusing it with cystic canal. Surgical skill and experience, misevaluation of anatomical structures during surgery, local operative risk factors (local inflammation, bleeding, obesity, hepatic cirrhosis, scleroatrophic gall bladder, hepatic neoplasms, Mirizzi’s syndrome, obesity, and penetrating duodenal ulcer), and aberrant anatomy are the major risk factors for injury [10, 11, 12]. Bile injuries during cholecystectomy may result in bile leakage, bile strictures, or both. The most common types of leakage after cholecystectomy are the cystic stump leakages and low-grade, spontaneously closing leaks seen in Luschka canals. Major bile duct injuries involving the common hepatic duct and common bile duct usually result in high-grade leakages [13, 14, 15].

The most common signs and symptoms include abdominal pain, jaundice, fever, ascites, and bilomas. Most cases with bile leakage present within 1 week after surgery although this period may well extend to 3 months [9, 16, 17].

Bile leakage can be diagnosed by ultrasonography, computed tomography, magnetic resonance cholangiopancreatography (MRCP), scintigraphy, endoscopic retrograde cholangiopancreatography (ERCP), fistulography, percutaneous transhepatic cholangiopancreatography (PTC) and laparotomy. ERCP has recently been the most widely employed method for both diagnosis and treatment. The basic
principles of the endoscopic method include relieving pressure excess within the biliary system (via ES and/or biliary prosthesis [stent or NBD]), and removing bile from the leakage site by biliary prostheses. The most common factor for the success of endoscopic therapy is whether bile tree has lost its continuity. Strasberg type A, D injuries, type E injuries with incomplete incision, and aberrant canal injuries demonstrable via cholangiogram (Strasberg B,C,E5) can be treated by ERCP. Therapy to be applied during ERCP (ES and/or endobiliary prosthesis) is determined by the injury type determined by findings of cholangiography, leakage grade (low-grade vs high-grade), and other factors accompanying injury (common bile duct stones or strictures).

The most common cause of bile leakage in this study was cholecystectomy operation performed for bile stone disease, most of which were laparoscopic surgeries (64%, in 20 patients). The second most common cause was cystobiliary fistulas detected after hydatid cyst surgery (n=10, 32%).

In our study bile leakage after cholecystectomy most commonly occurred from cystic stump and gall bladder bed. Eighty percent (n=16) of cases had low-grade leakage and 90% (n=18) had Strasberg Type A injury. Almost all cases (95%, n=19) were treated with NBD or BS in addition to ES. Endoscopic therapy was successful in all cases. 10F plastic stent was used in two of the cases and 7F plastic stents were used in five cases treated by ES+BS. Stents were retrieved 4–6 weeks later in all cases. All cases treated for bile leakage after cholecystectomy were successfully treated in a single session. Successful endoscopic therapy in all of our cases may be explained by the majority of injuries being Strasberg Type A, low-grade injuries that were mostly treated by ES application.

Animal studies evaluating the pressure gradient between the common bile duct and duodenum after sphincterotomy or stent placement have shown that intrabiliary pressure was reduced more effectively in the stent placement group than the group that undergone ES alone [18, 19]. Other clinical and experimental studies have also revealed that biliary stent therapy in conjunction with ES was more effective than ES alone in eliminating oddi sphincter pressure [20, 21, 22].

Although different studies have provided conflicting data regarding the endoscopic therapy efficiencies of NBD and BS, general opinion suggests that they are equally effective. NBD may be preferred to BS in highly morbid cases in which a repeat control cholangiogram is contemplated [23]. There are no exact data about the correlation of the size and diameter of the prosthesis and the efficiency of endoscopic therapy. The therapy is individualized according to other factors (e.g. common bile duct stone, stricture, and risk of post-ERCP pancreatitis).

Bile fistula is the most common complication in liver hydatid cyst [24, 25]. Its postoperative incidence varies from 5% to 63% [24, 25, 26, 27]. High-output fistulas lasting more than 10 days in the postoperative period are defined as persistent biliary fistulas. Low-output fistulas may be closed spontaneously, without the need for an endoscopic intervention. ERCP is recommended in the case of obstructive signs in bile ducts caused by residual cystic materials, cholangitis, and development of postoperative persistent external biliary fistula. It can also be performed in a later stage when secondary sclerosing cholangitis or oddi fibrosis takes place. Using ES and/or endobiliary prostheses (ES or NBD) in ERCP reduces the pressure gradient between the biliary system and duodenum, diverting bile flow to duodenum. In our study patients successfully treated with ES and NBD. The efficiency of ERCP approaches 90% in cases with biliary fistula as in our study [28].

Some researchers have advocated that ES alone and removing cystic material in the common bile duct whenever present would suffice for treatment of hydatid cyst disease involving biliary system. However, many other researchers have recommended using biliary prostheses in addition to ES for a couple of days to weeks [28, 29, 30]. Adas et al. and Akçakaya et al. demonstrated that using biliary stent or NBD in conjunction with ES improved treatment success when biliary strictures or cholelithiasis accompanied high-output fistulas [28, 30]. Çiçek et al. recommended NBD use owing to its properties of reducing intrabiliary pressure more
efficiently and enabling intraoperative detection of the localization of cystobiliary communication when applied at the preoperative period [31].

In the present study 10 patients with biliary fistula after hydatid cyst surgery were treated by ERCP. Three of the cases were detected to have an accompanying papillary stenosis. One case treated by ES alone. Endoscopic therapy was applied surgical therapy for concurrent persistent chronic fistula. One case presenting with low-output persistent fistula was treated by ES alone.

In conclusion, our study showed that ERCP is an effective method for the diagnosis and treatment of post-surgical bile fistula. Endoscopic therapy should be individualized on the basis of the etiology, fistula output, grade, and presence of other pathologies accompanying fistula.

Conflict of Interest: None declared.

Financial Disclosure: The authors declared that this study has received no financial support.

Authorship contributions: Concept – S.S., E.O.; Design – S.S., Supervision – S.S.; Data collection &/or processing – S.S., S.O., U.A., I.T., E.O.; Analysis and/or interpretation – S.S., K.O.; Literature search – S.S.; Writing – S.S., B.S., E.A.; Critical review – S.S., B.S., K.O., E.A.

REFERENCES

1. Roslyn JJ, Binna GS, Hughes EF, Saunders-Kirkwood K, Zinner MJ, Cates JA. Open cholecystectomy. A contemporary analysis of 42,474 patients. Ann Surg 1993;218:129–37. Crossref
2. Strasberg SM, Herlitz M, Soper NJ. An analysis of the problem of biliary injury during laparoscopic cholecystectomy. J Am Coll Surg 1995;180:101–25.
3. Adamsen S, Hansen OH, Funch-Jensen P, Schulze S, Stage JG, Wåra P. Bile duct injury during laparoscopic cholecystectomy: a prospective nationwide series. J Am Coll Surg 1997;184:571–8.
4. Bergman JJ, van den Brink GR, Rauws EA, de Wit L, Obertop H, Huijbregts K, et al. Treatment of bile duct lesions after laparoscopic cholecystectomy. Gut 1996;38:141–7. Crossref
5. Martin RF, Rossi RL. Bile duct injuries. Spectrum, mechanisms of injury, and their prevention. Surg Clin North Am 1994;74:781–807.
6. Sandha GS, Bourje MJ, Haber GB, Kortan PP. Endoscopic therapy for bile leak based on a new classification: results in 207 patients. Gastrointest Endosc 2004;60:567–74. Crossref
7. Roy PG, Soonawalla ZF, Grant HW. Medicolegal costs of bile duct injuries incurred during laparoscopic cholecystectomy. HPB (Oxford) 2009;11:130–4. Crossref
8. Larson GM, Virale GC, Casey J, Evans JS, Gilliam G, Heuser L, et al. Multipractice analysis of laparoscopic cholecystectomy in 1,983 patients. Am J Surg 1992;163:221–6. Crossref
9. Scott TR, Zucker KA, Bailey RW. Laparoscopic cholecystectomy: a review of 12,397 patients. Surg Laparosc Endosc 1992;2:191–8.
10. Krähenbühl L, Scabas G, Wente MN, Schäfer M, Schlumpf R, Büchler MW. Incidence, risk factors, and prevention of biliary tract injuries during laparoscopic cholecystectomy in Switzerland. World J Surg 2001;25:1325–30. Crossref
11. Moossa AR, Mayer AD, Stabile B. Iatrogenic injury to the bile duct. Who, how, where? Arch Surg 1990;125:1028–31. Crossref
12. Barkun AN, Rezeg M, Mehra SN, Pavone E, Landry S, Barkun JS, et al. Postcholecystectomy bile leaks in the laparoscopic era: risk factors, presentation, and management. McGill Gallstone Treatment Group. Gastrointest Endosc 1997;45:277–82.
13. Kitami M, Murakami G, Suzuki D, Takase K, Tsuibo M, Saito H, Takahashi S. Heterogeneity of subvesical ducts or the ducts of Luschka: a study using drip-infusion cholangiography–computed tomography in patients and cadaver specimens. World J Surg 2005;29:217–23. Crossref
14. Ko K, Kamiya J, Nagino M, Oda K, Yuasa N, Arai T, et al. A study of the subvesical bile duct (duct of Luschka) in resected liver specimens. World J Surg 2006;30:1316–20. Crossref
15. Rerknimitr R, Sherman S, Fogel EL, Kalayci C, Lumeng L, Chalasani N, et al. Biliary tract complications after orthotopic liver transplantation with choledochocholedochostomy anastomosis: endoscopic findings and results of therapy. Gastrointest Endosc 2002;55:224–31. Crossref
16. Davidoff AM, Branum GD, Meyers WC. Clinical features and mechanisms of major laparoscopic biliary injury. Semin Ultrasound CT MR 1993;14:338–45. Crossref
17. Davidoff AM, Pappas TN, Murray EA, Hilleren DJ, Johnson RD, Baker ME, et al. Mechanisms of major biliary injury during laparoscopic cholecystectomy. Ann Surg 1992;215:196–202.
18. Tantia O, Jain M, Khanna S, Sen B. Iatrogenic biliary injury: 13,305 cholecystectomies experienced by a single surgical team over more than 13 years. Surg Endosc 2008;22:1077–86. Crossref
19. Katsinopoulos P, Kountouras J, Paroutoglou G, Chatzinavroudis G, Germanidis G, Zavos C, et al. A comparative study of 10-Fr vs. 7-Fr straight plastic stents in the treatment of postcholecystectomy bile leak. Surg Endosc 2008;22:101–6. Crossref
20. Youngeeln MA, Marks JM, Ponsky T, Ponsky JL. Comparison of bile duct pressures following sphincterotomy and endobiliary stenting in a canine model. Surg Endosc 1997;11:126–8. Crossref
21. Kim KH, Kim TN. Endoscopic management of bile leakage after cholecystectomy: a single-center experience for 12 years. Clin Endosc 2014;47:248–53. Crossref
22. Manouras A, Genetzakis M, Antonakis PT, Lagoudianakis E, Patras M, Papadima A, et al. Endoscopic management of a relapsing hepatic hydatid cyst with intrabiliary rupture: a case report and review of the literature. Can J Gastroenterol 2007;21:249–
53. Crossref

23. Galati G, Sterpetti AV, Caputo M, Adduci M, Lucandri G, Brozzetti S, et al. Endoscopic retrograde cholangiography for intra-biliary rupture of hydatid cyst. Am J Surg 2006;191:206–10.

24. Somani SK SA. Resolution of Hepatic Hydatid Cyst with Biliary Communication with ERCP. J Gastroint Dig Syst 2012;2:114.

25. Kayaalp C, Bzeizi K, Demirbag AE, Akoglu M. Biliary complications after hydatid liver surgery: incidence and risk factors. J Gastrointest Surg 2002;6:706–12. Crossref

26. El Malki HO, El Mejdoubi Y, Souadka A, Mohsine R, Ifrine L, Abouqal R, et al. Predictive model of biliocystic communication in liver hydatid cysts using classification and regression tree analysis. BMC Surg 2010;10:16. Crossref

27. de Aretxabala X, Perez OL. The use of endoprostheses in biliary fistula of hydatid cyst. Gastrointest Endosc 1999;49:797–9. Crossref

28. Adas G, Arikan S, Gurbuz E, Karahan S, Eryasar B, Karatepe O, et al. Comparison of endoscopic therapeutic modalities for postoperative biliary fistula of liver hydatid cyst: a retrospective multicentric study. Surg Laparosc Endosc Percutan Tech 2010;20:223–7. Crossref

29. Sharma BC, Reddy RS, Garg V. Endoscopic management of hepatic hydatid cyst with biliary communication. Dig Endosc 2012;24:267–70. Crossref

30. Akcakaya A, Sahin M, Karakelleoglu A, Okan I. Endoscopic stenting for selected cases of biliary fistula after hepatic hydatid surgery. Surg Endosc 2006;20:1415–8. Crossref

31. Cicek B, Parlak E, Disibeyaz S, Oguz D, Cengiz C, Sahin B. Endoscopic therapy of hepatic hydatid cyst disease in preoperative and postoperative settings. Dig Dis Sci 2007;52:931–5. Crossref