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## An algorithm for the treatment of the biliary complications of hepatic hydatid disease

**Aim:** The treatment of hepatic hydatid disease (HHD) is currently standardized. Biliary complications of HHD complicate both the treatment and course of the disease. Several investigations have been performed on the biliary complications of HHD and their treatment. We propose an algorithm for the treatment of the biliary complications of HHD based on our experience.

**Materials and methods:** We investigated 148 patients that underwent endoscopic retrograde cholangiopancreatography (ERCP) due to complicated HHD between January 2000 and December 2006 at the endoscopy unit of the Department of Surgery of Atatürk University Medical School. Age, sex, indications for ERCP and endoscopic sphincterotomy (ES), ERCP findings, laboratory data, operative findings, postoperative complications, and additional interventions (surgical or percutaneous) were noted.

**Results:** Twenty-six patients had not previously undergone surgery for HHD. While 23 of these patients underwent ERCP preoperatively, 3 underwent ERCP during both the pre- and postoperative periods. The remaining 122 patients underwent surgery for HHD and ERCP during the postoperative period.

Indications for preoperative ERCP were cholangitis and various clinical signs of cysto-biliary communication (CBC), such as abnormal liver function test results (bilirubin, ALT, AST, GGT, and ALP), biliary colic, and obstructive jaundice. In this group of patients ERCP/ES was not successful in 2 patients that underwent surgery due to emergent circumstances, and another 3 patients developed postoperative biliary fistulae.

Indications for postoperative ERCP were persistent bile leakage after surgical treatment for HHD, postoperative hyperbilirubinemia and cholangitis, and postoperative biloma formation in the cystic cavity. All patients with cholangitis experienced relief of symptoms after ERCP and ES, 1 patient with biloma formation and 5 patients with persistent biliary fistulae were operated on.

**Conclusion:** ERCP and ES are highly effective in the treatment of the biliary complications of HHD. Repeat ERCP should be performed in patients that do not respond to the first intervention.

**Key words:** Hepatic hydatid disease, persistent biliary leakage, biloma, ERCP

### Karaciğer hidatik hastalığının biliyer komplikasyonlarının tedavisi için bir algoritma

**Amaç:** Karaciğer hidatik hastalığının (KHH) tedavisi artık standardize edilmiştir. KHH'nin safra yolunda oluşturduğu komplikasyonlar hem tedaviyi hem de hastalığın seyrini komplike hale getirmektedir. KHH'nin biliyer komplikasyonları ve tedavisi hakkında çok sayıda çalışmalar yapılmıştır. Biz bu çalışmada KHH'nin biliyer komplikasyonlarının tedavisi üzerine kendi deneyimlerimize dayalı bir algoritma öne sürdük.

**Yöntem ve gereçler:** Ocak 2000 ile Aralık 2006 tarihleri arasında Atatürk Üniversitesi Tıp Fakültesi Genel Cerrahi AD, Endoskopi Ünitesinde 148 hastaya komplike KHH için endoskopik retrograd kolanjio- pankreatografi (ERKP) yapıldı. Hastaların yaşları, cinsiyetleri, ERKP ve endoskopik sfinkterotomi (ES) endikasyonları, laboratuvar verileri, ameliyat bulguları, ameliyat sonrası komplikasyonlar ve başka girişimler (cerrahi veya perkütan) kaydedildi.

**Bulgular:** Yirmi altı hasta daha önceden KHH için ameliyat olmamıştı. Bunları 23'üne ameliyattan önce 3'üne ise hem ameliyattan önce hem de ameliyattan sonra ERKP yapıldı. Geri kalan 122 hasta ise KHH nedeniyle ameliyat edilmiş hastalardı ve bunlara ameliyattan sonraki dönemde ERKP yapıldı.

Received: August 22, 2008  
Accepted: May 13, 2008

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Ameliyat öncesi dönemde ERKP endikasyonları kolanjit ve kisto-biliyer iştirake ait, karaciğer fonksiyon testlerinde (bilirubin, ALT, AST, GGT, ALP) anormallikler, biliyer kolik ve tıkanma sarılığı gibi klinik bulguların varlığıydı. Bu grupta 2 hastada ERCP/ES başarılı olmadı ve bu hastalar acil şartlarda ameliyat edildi ve başka 3 hastada ameliyattan sonra safra fistülü gelişti.

Ameliyat sonrası dönemde ERKP için endikasyonlar KHH'nın cerrahi tedavisinden sonra persistan safra fistülü, ameliyat sonrası bilirubin yükselmesi ve kolanjit ve kist boşluğunda ameliyat sonrasında biloma oluşmasıydı. Kolanjitli tüm hastalarda ERKP ve ES sonrası semptomlar geriledi, bilomalı bir hasta ve persistan safra fistülü olan 5 hasta ameliyat edildi.

**Sonuç:** Biz KHH'nın biliyer komplikasyonlarının tedavisinde ERKP ve ES'nin çok etkili olduğu sonucuna vardık. İlk girişime cevap vermeyen hastalarda ERKP tekrar edilmelidir.

**Anahtar sözcükler:** Karaciğer hidatik kist hastalığı, persistan safra kaçağı, biloma, ERKP

## Introduction

Hydatid disease is endemic in many parts of the world. The disease most commonly affects the liver, and treatment of hepatic hydatid disease (HHD) is currently standardized. While surgery is the mainstay of radical treatment and has the potential for a complete cure, other treatments, such as PAIR (puncture, aspiration, injection, and re-aspiration) and chemotherapy with benzimidazole compounds, have limited utility. Depending on the individual case, each of these therapeutic modalities has potential as well as limitations of varying degrees. Although chemotherapy is a noninvasive treatment, its success is limited as a single measure, and thus it is used in addition to other therapeutic modalities (1).

Complications of HHD are primarily the result of its effect on the biliary tree. Indeed, biliary rupture is one of the most common complications and can vary between small cysto-biliary communication (CBC) to large intrabiliary rupture (2). Biliary rupture can complicate the course of the disease, during both the pre- and postoperative periods. Preoperatively, biliary obstruction can cause cholangitis and obstructive jaundice. During the postoperative period it can cause biliary fistulae, which can be difficult to manage. Therapeutic endoscopic retrograde cholangiopancreatography (ERCP), including endoscopic sphincterotomy (ES), and balloon and basket extraction, are the first choices of treatment in patients with biliary complications of HHD. In the present study we report our experience with the use of ERCP in the treatment of HHD and define an algorithm for the treatment of HHD with biliary complications.

## Materials and methods

We used data obtained from 148 patients that underwent ERCP for complicated HHD between January 2000 and December 2006 at the endoscopy unit of the Department of Surgery of Atatürk University Medical School. Age, sex, indications for ERCP and ES, ERCP findings (contents of the CBD, communication with the cystic cavity), and laboratory data (bilirubin, alanine amino transferase [ALT], aspartate amino transferase [AST], gamma-glutamyl transferase [GGT], and alkaline phosphatase [ALP] levels, operative findings, postoperative complications [duration and amount of biliary drainage] and additional interventions [surgical or percutaneous]) were noted. Indications for ERCP and ES were described as laboratory findings that indicated CBC preoperatively, preoperative biliary complications (cholangitis, obstructive jaundice), postoperative persistent biliary leakage, and biloma and cholangitis. Postoperative persistent bile leakage was described as continuous bile discharge from a lodge drain for more than 10 days (3).

Study patients were kept nil per os (NPO) during the night before the procedure. While in the prone position patients were intravenously administered sedative premedication, which consisted of midazolam 0.05 mg kg<sup>-1</sup> and pethidine HCl 0.5 mg kg<sup>-1</sup>; these patients were closely monitored via pulse oximetry.

ERCP was performed with therapeutic endoscopes (Olympus TJF 240, Tokyo, Japan), using standard ERCP catheters and sphincterotomes. A balloon-occluded cholangiogram was obtained to demonstrate subtle communication when communication was not

observed with routine cholangiography. ES, followed by the extraction of the cyst membrane or daughter cysts, was performed as indicated. All patients that underwent surgery in our clinic received preoperative albendazole treatment ( $10 \text{ mg kg}^{-1}$ ) 15 days before the operation and 2 months postoperatively (according to the surgeon's preferences). The decision to perform ERCP or ES, pre- or postoperatively, was also made according to the surgeon's preferences. Operative procedures were also chosen by the surgeon.

Surgeons from other hospitals were invited to share their data and report their patients' complications and outcomes during the follow-up period. The duration of the follow-up period was between 6 and 70 months. In all, 126 patients were followed-up at our clinic and 22 were followed by surgeons at other hospitals. Follow-up data were obtained from 117 patients.

The data were analyzed using SPSS v.12.0 (SPSS, Chicago, IL, USA). Analysis was performed using Student's t test for continuous variables, and chi-square or Fisher exact tests for categorical variables. Pearson's correlation analysis was used to determine the correlations between the duration of fistulae, and the daily output and timing of ERCP, between the size of the cysts and closure time, between the size of the cysts and daily bile output, and between the amount of daily output and duration of closure.  $P < 0.05$  was considered statistically significant.

## Results

In total, 148 patients that underwent ERCP and ES for complicated HHD between January 2000 and December 2006 at the endoscopy unit of the Department of Surgery of Atatürk University Medical School were included in the study. During this period 1532 ERCPs were performed in our endoscopy unit; 26 of the patients had not previously undergone surgery for HHD. While 23 of the patients underwent ERCP preoperatively, 3 underwent ERCP during both the pre- and postoperative periods. The remaining 122 patients had surgery for HHD and underwent ERCP during the postoperative period.

### Preoperative ERCP

Nine patients underwent preoperative ERCP and ES for the treatment of cholangitis. In the remaining

17 patients ERCP and ES were performed to address various clinical signs of CBC, such as abnormal liver function test results (bilirubin, ALT, AST, GGT, and ALP), biliary colic, and obstructive jaundice. Mean age of patients that underwent preoperative ERCP was 35.6 years (range: 12-67 years). Twenty patients had 1 cyst and the other 6 patients had 2 cysts (total: 32 cysts). Mean diameter of the cysts was  $8.3 \pm 4.1 \text{ cm}$  (range: 3-16 cm). Twenty of the cysts had a diameter larger than 10 cm, and 22 cysts were located on the right lobe and the remaining 10 were located on the left lobe. Twelve cysts were located on the caudate lobe, and segments 4 and 5.

All patients in the preoperative ERCP group underwent ERCP and ES. Successful cannulation of the common bile duct was initially performed in 22 patients, followed by another 4 patients. The diameter of the common bile duct (CBD) ranged from 6 to 38 mm. There were no positive findings in 4 of the patients. In 2 of the patients the CBD was compressed and distorted by the cysts. In the remaining 20 patients cystic contents, germinative membranes, and purulent material were drained from the CBD.

Additionally, 4 of the patients underwent a second ERCP (3 with cholangitis, 1 with obstructive jaundice). In 24 patients symptoms resolved after the first or second endoscopic intervention. In 2 of the patients with cholangitis, the clinical signs did not resolve and they were operated on under emergency circumstances.

All patients in this group were operated on (24 elective and 2 emergency). Eight patients had infected cystic contents and bile in their cysts. Cystic cavities were explored for possible bile duct openings, and in 4 patients openings were found and sutured (Figure 1). In the patients that underwent emergency surgery, CBD exploration was performed during the procedure, in addition to the management of the cyst and cystic cavity (Figure 2). A choledocoduodenostomy was also performed in the 2 patients that were operated on under emergency conditions.

Overall, persistent postoperative bile leakage developed in 3 (11.5%) of these patients.

### Postoperative ERCP

In total, 125 patients underwent ERCP during the postoperative period (including 3 patients that

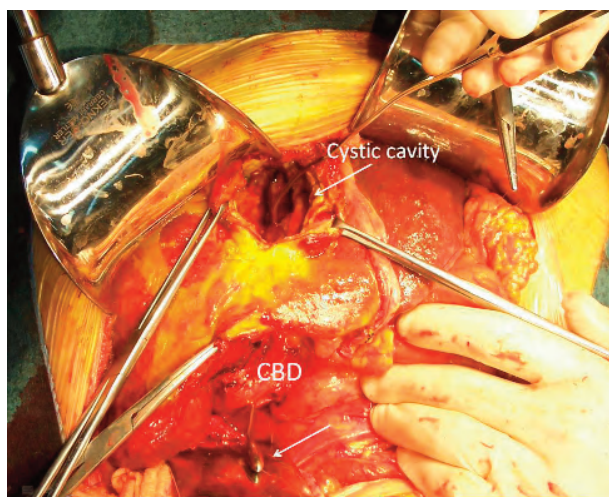


Figure 2. Intraoperative photo shows hydatid membrane extraction from the common bile duct.



Figure 1. Intraoperative demonstration of communication between the cystic cavity and the bile duct. Arrow indicates the tip of the boogie introduced from the CBD into the cystic cavity.

underwent preoperative ERCP at our clinic). Persistent bile leakage after surgical treatment for HDD in 99 patients, postoperative hyperbilirubinemia and cholangitis in 12 patients, and postoperative biloma formation in the cystic cavity in 14 patients were the indications for postoperative ERCP.

**Postoperative cholangitis**

Twelve patients underwent ERCP and ES for postoperative cholangitis. All had elevated liver function test results, hyperbilirubinemia, fever, and leukocytosis. There were no signs of biliary leakage or bile accumulation in the cyst cavity or in the

abdomen. Mean CBD diameter at the time of ERCP was 12.2 mm (range: 8-21 mm). ERCP demonstrated CBC in 2 patients (Figure 3) and choledocholithiasis (extracted with balloon catheter) in 1 patient. The remaining patients had purulent material in the CBD, which was promptly drained. ES was performed in all of these patients. In all patients the signs and symptoms of cholangitis resolved after ERCP and ES, without the need for additional ERCP/ES or surgery. There was rapid relief of symptoms, within a mean of 1.2 days (range: 1-4 days).

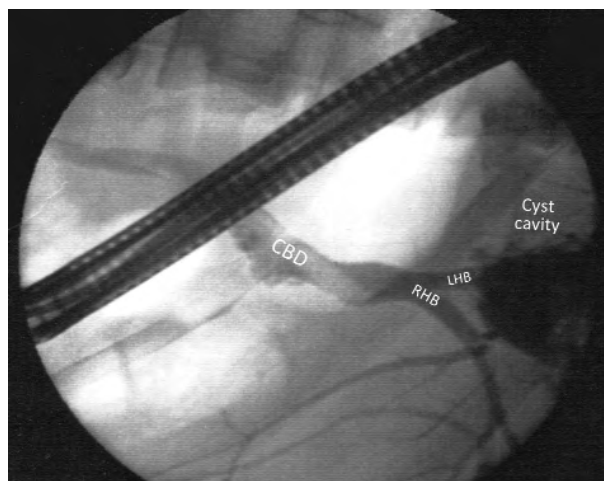


Figure 3. ERCP image shows communication between the bile duct and cystic cavity.

**Postoperative biloma**

Fourteen patients underwent ERCP and ES for bilomas in the cystic cavity. In 10 of the patients percutaneous drainage of the cavity, prior to ERCP, was performed. In 4 of the patients, percutaneous drainage was not technically possible because of the localization of the cyst. In all, 5 patients underwent repeat ERCP/ES.

Mean CBD diameter at the time of ERCP was 13.4 mm (range: 8-19 mm). ERCP demonstrated CBC in 8 of the patients. In 6 of the patients there were no positive findings at the time of ERCP.

In 13 patients ERCP/ES alone, or in combination with percutaneous drainage, was effective and the bilomas completely resolved. (Figures 4-6) In 1 patient (who was percutaneously drained) the biloma did not resolve and a cavity infection developed. This patient

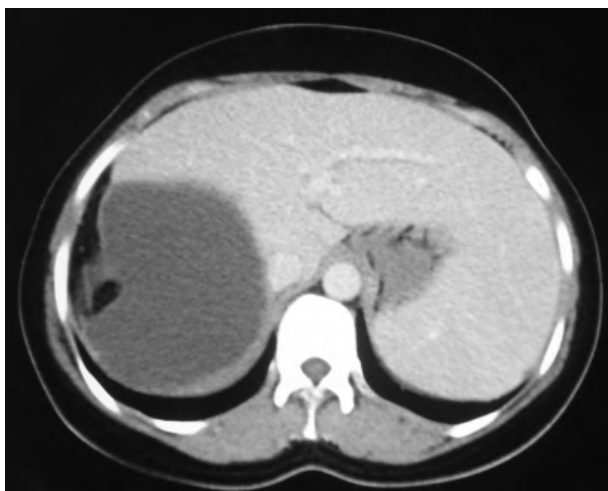


Figure 4. Axial CT scan shows the formation of a large biloma in the operated cystic cavity on the right lobe of the liver.

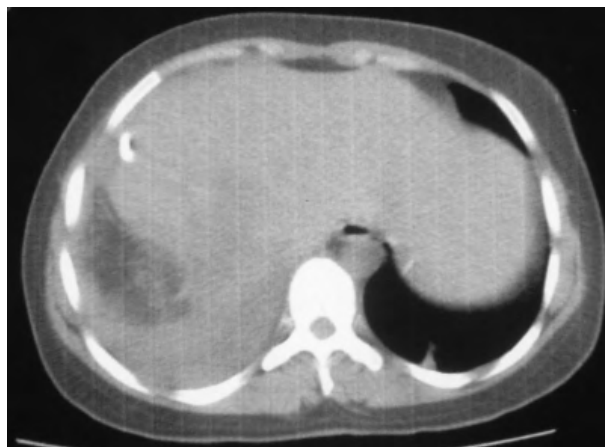


Figure 6. Axial CT scan shows a collapsed cystic cavity after drainage of the biloma within the cavity.

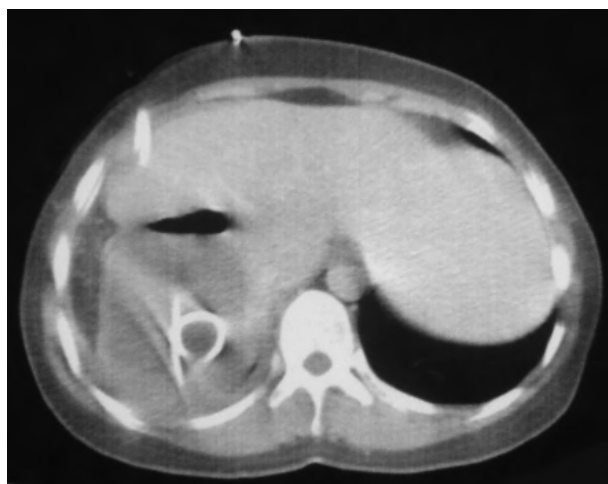


Figure 5. Axial CT scan shows a biloma drained percutaneously.

then underwent a right hepatectomy. Mean time of cyst resolution was  $21 \pm 12$  days (range: 6-39 days).

#### Postoperative biliary leakage

Ninety-nine patients with persistent bile leakage after surgical treatment for HHD underwent ERCP/ES. Of these patients, 77 were operated on at our clinic and 22 were operated on at different clinics, but were referred to our department for additional interventions. Four patients had 3 cysts, 12 had 2 cysts, and 83 had only 1 cyst (total cysts: 119). Mean cyst diameter in this group was  $8.6 \pm 6.1$  cm. In 57 (57.5%) of the patients the cyst associated with bile leakage was larger than 10 cm. There was a positive

correlation between the size of the cyst and closure time ( $P = 0.04$ ,  $r = 0.4$ ). There was no correlation between the size of the cyst and daily bile output ( $P < 0.05$ ). Of the 119 cysts, 18 (15.1%) were located on the left liver lobe and 101 (84.9%) on the right liver lobe. Twenty-two of the patients in this group had not received albendazole pre-treatment (13 were operated on at another clinic, 2 were pregnant, and 7 were allergic to albendazole). Four patients were operated on in an emergency setting due to a free intraperitoneal rupture. Forty-four of the cysts contained infected material and bile, while the remaining cysts were free of these contents. CBC was demonstrated in 19 (19.1%) of the cysts, which were sutured intraoperatively.

During the postoperative period 57 patients (57.5%) had elevated ALP and GGT levels, 21 patients (21.1%) had, in addition, elevated ALT, AST, and bilirubin levels. The remaining 42 patients (42.4%) had normal levels of ALP, AST, ALT, GGT, and bilirubin.

Biliary drainage began on the 1st day in 49 of the patients (49.4%), on the 2nd day in 30 patients (30.3%), and on the 3rd day in 20 patients (21.3%). Mean drainage was  $475 \pm 215$  cc (range: 80-1400 cc). There was a positive correlation between the daily output and closure time ( $P = 0.01$ ,  $r = 0.04$ ). ERCP was performed between the 8th and 47th postoperative days, with a mean of 17.2 days. In 38 patients (38.3%) ERCP/ES was performed within 20

days postoperatively, and in the remaining 61 patients (61.7%) it was performed after the 20th postoperative day. All patients underwent ES. There was a positive correlation between the timing of the ERCP and duration of closure ( $P = 0.01$ ,  $r = 0.2$ ). Selective CBD catheterization was successful in 79 (79.8%) patients during a first attempt and in 20 patients during a second attempt. Two patients had periampullary diverticula.

Mean CBD diameter was  $14.2 \pm 5.4$  mm (range: 6-28 mm). In 85 patients (85.8%) there were cystic contents, purulent material, infected bile, or sludge in the CBD, which was extracted after ES. One patient had choledocholithiasis, which was also extracted. In 13 (13.1%) patients the CBD was less than 8 mm in diameter and was empty. CBC was observed in 79 (79.7%) of the patients.

Of the patients with postoperative biliary fistulae, 94 benefitted from ERCP/ES (94.9%). Twenty-one patients required a second ERCP/ES and 9 required a third ERCP/ES. In all patients with postoperative biliary fistulae, daily fistula output decreased after the 1st, 2nd, or 3rd endoscopic intervention; however, biliary drainage did not end in 5 of the patients. The time between the first and second ERCP varied between 11 and 21 days (mean: 13.1 days). A decrease in biliary drainage after ERCP and ES was evident after 2.4 days (range: 1- 18 days); biliary drainage ended in a mean of 5.2 days (range: 2-57 days).

Five patients were re-operated on for persistent biliary fistulae after the first operation. One patient received a cystojejunostomy, 1 received a right hepatectomy, and 3 received a pericystectomy.

### Complications

The overall complication rate was 0.4% (6 patients). One patient suffered from bleeding related to ES, 4 patients had pancreatitis, and 1 developed cholangitis after ERCP and ES. There were no perforations related to ERCP or ES among the 148 patients. In 16 patients transient elevated amylase, not associated with pancreatitis, was observed.

### Follow-up period

We were able to collect follow-up data from 79 (53.3%) of the 148 patients. Mean follow-up period was 31.3 months (range: 12-84 months). Fourteen patients were readmitted to our clinic: 5 for recurrent

hydatid disease, 3 for obstructive jaundice, 3 for cholangitis, 1 for liver abscess, and 1 for persistent pain at the operation site (right upper quadrant).

There were no positive findings in the patient with persistent pain and no treatment was given. The patient with liver abscess at the residual cavity was treated with percutaneous drainage and repeat ERCP and ES. The hepatic abscess resolved 14 days after the ERCP/ES.

Three patients with recurrent hydatidosis were treated percutaneously and the other 2 were operated on. None of these patients had repeat ERCP/ES.

All of the patients with cholangitis and obstructive jaundice underwent repeat ERCP/ES. There was no CBC in these patients. Purulent material and sludge were drained from the CBD in patients with cholangitis, as well as from 2 patients with obstructive jaundice. One patient with obstructive jaundice had a deformed and twisted CBD. This patient was treated with biliary stenting and bilio-enteric diversion (hepaticojejunostomy).

### Discussion

CBC, communication between the cyst and the biliary tree, is classified as major and minor (4). It is also defined as an intrabiliary rupture and is among the most common complications of hydatid cysts of the liver. Major (or frank) rupture is defined as cystic contents draining directly into a major biliary duct, causing intermittent or complete obstruction of the duct, thereby causing symptoms and laboratory abnormalities. Minor (occult or simple) ruptures can be asymptomatic and can become postoperative bilio-cutaneous fistulae, unless they are properly sutured at the time of surgery (5). While the true incidence rate of CBC is unknown, several studies report incidence rates between 5% and 37%. The incidence rate of frank intrabiliary rupture is reported to range between 5% and 17% (2,6-15). The criteria for CBC are visualization of a cysto-biliary opening during surgery or demonstration of communication by ERCP in patients with hydatid jaundice or biliary leakage after hydatid surgery of the liver (16).

It is reported that pressure within the hydatid cyst that is higher than the bile pressure, fragility of the parasitic wall, and proximity of the cyst to a major

biliary duct are the main factors responsible for rupture of the cyst into the biliary tree (5).

CBC complicates the treatment of HHD. During the preoperative period CBC can cause infection of the cyst, thereby forming an infected cyst and abscess. Drainage of the cystic contents into the biliary tree then causes obstructive jaundice and even cholangitis. During the postoperative period the main problem is bile leakage or bile fistulae. Biliary fistulae develop when the postoperative leak is able to drain; if not, biliary peritonitis and biliary abscesses develop (16).

In the present study we experienced the therapeutic use of ERCP in preoperative settings, but preoperative ERCP has both diagnostic and therapeutic uses. The use of ERCP in all patients with HHD, including asymptomatic patients, remains controversial because there are limitations to the diagnostic utility of ERCP in this setting. It is reported that due to increased pressure within the cyst, minimal extent of communication, or transient obstruction of the aperture from a superimposed daughter cyst, small CBCs cannot be seen in some cases. Moreover, on rare occasions an intrahepatic biliary tree may not be filled because of the extrinsic mass effect of the hydatid cyst at the hilum of the liver. Indeed, the false-negative rate of this condition may be as high as 17%-20% (17,18). Ozaslan et al. (2) reported that daughter cysts, or hydatid material within the common bile duct, may not always be detected (2). Yet another important issue is complications of ERCP. Although complication rates are reported to be low, these rates are expected to rise due to the known inherent risks of therapeutic ERCP procedures (19). Despite these limitations, it is reported that in 25%-50% of asymptomatic patients ERCP can identify features compatible with CBC (17).

We used ERCP to preoperatively treat complications in patients with HHD. All patients were symptomatic and had elevated liver enzymes, and the indications were cholangitis, obstructive jaundice, and biliary colic. The use of preoperative ERCP is mostly recommended in symptomatic patients (2,17,20,21). CBC and obstruction due to daughter cysts or hydatid material detected during cholangiography can be managed by preoperative therapeutic ERCP, including sphincterotomy, balloon and basket extraction, nasobiliary drainage (NBD), or stent

insertion; the success rate is reported to be between 80% and 100% (4,10,22-32). Other researchers suggest the use of stents or NBD during the preoperative period, just for symptom relief and avoidance of postoperative biliary fistulae (2,33). It is proposed that in some cases (up to 25% in some series) there is no need for elective surgical treatment after endoscopic intervention. Moreover, insertion of an NBD and irrigation of the cystic cavity with hypertonic saline are suggested (21,34); however, we did not use NBD and did not experience spontaneous cyst resolution.

In the presented series preoperative ERCP and ES failed in 2 patients with cholangitis, despite repeat ERCP. These 2 patients underwent emergency surgery and CBD exploration was performed. The remaining patients underwent elective ERCP and ES. Preoperative ES in order to avoid postoperative external fistulae is also recommended. Rodriguez et al. (28) reported that none of their patients developed postoperative persistent fistulae after preoperative sphincterotomy (8 cases) (28); however, 3 (11.5%) of our 26 preoperative ERCP patients developed persistent biliary fistulae following elective surgery and postoperatively underwent repeat ERCP/ES. Thus, the cystic cavity should be examined for biliary openings, even if preoperative ES is performed.

How can the risk of biliary leakage from CBCs be evaluated preoperatively, and what should be done intraoperatively? In order to reduce postoperative bile leaks, all efforts should be made, both preoperatively and during surgery, to detect CBCs. An intraoperative cholangiogram may also be useful (16,35). This intraoperative cholangiogram could be made via a t-tube or a preoperatively placed NBD during the operation (35). While a choledochotomy for placement of a t-tube seems invasive, a less invasive procedure could be to place an NBD prior to surgery, as this could be used to perform a cholangiogram during and after the operation. Indeed, it can be useful during the operation for detecting small CBCs. Yet the placement of an NBD is not entirely harmless, as it is uncomfortable for the patient and has the potential for stricture formation.

Postoperative complications for patients with HHD include the formation of bilomas, cholangitis, and persistent biliary leakage. Cholangitis may

develop after HHD surgery and can be present in 11% of patients that develop biliary fistulae after HHD surgery (5). Lee et al. (36) compared the use of a stent and NBD for the early decompression of the CBD in acute cholangitis. While they found that the 2 methods were equally effective, they reported that NBD was less comfortable (36). In 12 of our patients ERCP and ES were performed for the treatment of cholangitis. The efficacy of ERCP and ES in these patients was high, and there was no need for further surgical or endoscopic treatment.

Another complication is postoperative biloma formation. In 14 patients we observed bilomas at the residual cavity of the HHD. This occurs when there is CBC and the cavity is not properly drained. ERCP and ES were performed for the management of this condition. Percutaneous drainage was performed in 10 patients that were suitable for this approach. Christoforidis et al. (37) investigated the use ERCP/ES, and stent and NBD insertion combined with percutaneous treatment in post-cholecystectomy bilomas and reported that it was effective (37). In the present study ERCP and ES alone, or in combination with percutaneous drainage, was also effective in the treatment of bilomas after HHD. We recommend the use of percutaneous drainage combined with ES, if possible.

The most common postoperative complication of hepatic hydatid cyst surgery is external biliary fistulae. Biliary fistulae occur in 4%-9% of cases. A persistent external biliary fistula is defined as a fistula that persists after the tenth postsurgery day. Although spontaneous closure may occur, persistent biliary fistulae are not infrequent (38). Bile leakage can complicate the postoperative period in patients that undergo surgery for HHD. It is reported that postoperative biliary leakage significantly increases postoperative complications (16); it significantly increases the length of postoperative hospital stays, as reported by Kayaalp (3), Demircan (16), and Atli (39) (3,16,39). We were not able to compare the length of hospital stays (LOS) between HHD patients with and without biliary fistulae.

Development of a connection between the cyst and the biliary tree is the main cause of fistulae. Cystic growth into the liver parenchyma erodes the adjacent bile duct and forms a communication between the

cystic cavity and biliary tree. This connection makes it possible for hydatid material to enter the biliary tree or for bile to leak into the cyst. When there is communication between the biliary tract and the residual cyst cavity, bile may flow from the biliary tree into the cystic cavity as a result of the pressure gradient formed after surgery. This can be aggravated by stenosis of the sphincter of Oddi or occlusion of the CBD by hydatid material (38).

Some predictors of postoperative biliary fistulae are described as follows: Demircan et al. reported that ALP concentrations greater than  $250 \text{ U L}^{-1}$ , a total bilirubin level above  $17.1 \mu\text{mol L}^{-1}$ , direct bilirubin above  $6.8 \mu\text{mol L}^{-1}$ , GGT higher than  $34.5 \text{ U L}^{-1}$ , and cyst size greater than 8.5 cm in the preoperative period were independent predictors of occult CBC; ALP was the most important (16). Atli et al. (39) reported that elevated ALP and direct bilirubin were risk factors for occult CBCs, and Kayaalp et al. (3) reported that high ALP and GGT levels were risk factors for CBCs (3,39). In the present study, 42 patients (42.4%) had normal levels of ALP, AST, ALT, GGT, and bilirubin during the postoperative period. The remaining 57 patients (57.5%) had elevated ALP and GGT levels, while 21 of them (21.1%) had elevated ALT, AST, and bilirubin levels. Our study was not designed to identify the predictors of postoperative biliary fistulae in patients undergoing surgery for HHD and, therefore, we were unable to compare the laboratory test results of the patients that developed fistulae and non-complicated HHD patients; however, the fact that 42.4% of patients with postoperative biliary fistulae had normal liver function test results is noteworthy.

Mean cyst diameter in this group was  $8.6 \pm 6.1 \text{ cm}$ . In 57 (57.5%) patients, the cyst associated with bile leakage was larger than 10 cm. There was a positive correlation between the size of the cysts and closure time. Cyst diameter is suggested to be one of the predictors of biliary leakage. Several authors reported different cyst sizes as the cut-off point. While Demircan et al. (16) reported that cysts larger than 8.5 cm were an independent predictor of occult CBC, Atli et al. (39) reported that cysts 14.5 cm or greater in diameter independently predicted occult intrabiliary rupture. Bedirli et al. (15) observed a mean cyst diameter of 9 cm in 41 patients with intrabiliary



rupture. Among these researchers, a common finding is that large cysts are associated with biliary leakage. Yet Kayaalp et al. (13) reported that 65% of cysts that caused biliary leakage were less than 10 cm. Kayaalp's findings closely resemble those of the present study; in only 57.5% of patients with postoperative biliary leakage, the cyst associated with the fistula was larger than 10 cm. Kayaalp et al. (13) also stated that cysto-biliary complications, biliary leakage, and biliary fistulae were more common after resection in cysts localized near the hilum (3,13,15,16,39).

In a retrospective review reported from our clinic, Balik et al. (7) stated that postoperative biliary fistulae commonly close spontaneously within 2-4 months. In another series, spontaneous closure was reported to occur within 38 days (40). Although spontaneous closure may be expected, prolonged duration causes significant morbidity. Thus, endoscopic intervention is necessary.

The main aim of fistula treatment is to reduce pressure in the biliary tree. This pressure is reported to be less than 8-0 mm Hg (41,42). It is reported that reducing the pressure gradient between the bile duct and the duodenum, and diversion of bile away from the site of the leak result in healing of fistulae (43). This is provided by either surgical or endoscopic means. Surgically, common bile duct exploration, t-tube drainage, sphincteroplasty, or choledochoduodenostomy have frequently been employed during HHD surgery to prevent the development of biliary fistulae (44-46). These operative treatment modalities for biliary fistulae after HHD surgery are still used, but endoscopic interventions are replacing them. Currently, the use of ERCP is the gold standard for postoperative bile leakage and cholangitis (2).

Endoscopic drainage can be performed by endoscopic sphincterotomy (ES), nasobiliary drain, or stent insertion. There are no guidelines that definitely recommend when to choose ES, NBD, or stenting. We routinely performed ES in our patients with biliary leakage after HHD surgery. ES was also performed before surgery in patients with suspected CBCs.

Some reports recommend using only ES. ES is a one-step procedure that is generally more familiar to endoscopists, is less time consuming, and provides

extraction of retained material (2). Yet ES has limitations and is associated with complications, including bleeding and perforation of the sphincterotomy site. In our series we observed a few complications, the majority of which was pancreatitis. Bleeding occurred in only 1 patient and there was no perforation. For persistent biliary fistulae ES was an effective treatment in 94 (94.9%) patients in our series; however, there was a need for repeat ERCP in 21 patients and there were patients with prolonged fistulae (up to 2 months in 3 patients). Furthermore, 5 patients were operated on because endoscopic treatment failed. Saritas et al. (47) reported that the overall success rate of endoscopic treatment was 86% and that a second surgical intervention was required for only 6 of their patients. We think that repeat ERCP, combined with the patience to observe prolonged fistulae, can decrease the rate of surgical interventions performed for postoperative biliary leakage.

Although NDB and stenting are less invasive methods, ES is preferred by some surgeons in cases in which cystic contents are present in the bile ducts (48). Technically, a wide and satisfying ES can cause displacement of a stent or NBD, but if the ES is not wide enough it will not be possible to clear all the cystic contents from the CBD. Thus, the endoscopist must decide whether or not it is necessary to remove the cystic contents from the CBD. The mechanism that causes biliary complications of HHD depends mostly on occlusion of the CBD by cystic contents; therefore, it is more logical to remove these materials and create a free flow for the bile. Furthermore, in cases of Oddi stenosis, ES will provide a satisfactory decrease in pressure. Rodriguez et al. (28) and Tekant et al. (49) reported successful results using ES in their patients (28,49). Our experience also suggests that ES is safe and effective for the management of biliary complications of HHD.

Ozaslan et al. (2) suggest the use of NBD, stating various advantages (2). The introduction of the catheter above the defect allows continuous aspiration when the fistula originates at the level of the intrahepatic biliary tract. NBD also decreases pressure in the biliary tract, allows monitoring of fistulae by cholangiography, and is appropriate for patients with coagulopathy (2,43). The disadvantages of this approach are that NBD is less comfortable for the

Table 1. Indications for ERCP (note that 3 patients underwent ERCP both in the pre- and postoperative periods).

Indications	Preoperative ERCP	Postoperative ERCP
Cholangitis	9	12
Biloma	-	14
CBC or fistula	17	99
Total	26	125

patient, it can become displaced, and it can deprive the patient of a significant proportion of their intestinal bile (38,43). Cicek et al. (33) use NBD in their patients more often than is usually reported in the literature, and further suggest that NBD offers the following additional advantages: NBD decreases intraductal pressure more than ES or stenting, is more convenient for following-up leak closure via repeat cholangiograms, is more easy to remove after closure of the leak, is useful during surgery for detecting small

CBCs, and finally, is more useful when placed preoperatively. Nonetheless, these reported advantages should be investigated further, as we do not agree that these are valid advantages. To begin with, there is no evidence that NBD decreases pressure in the CBD more than stenting or ES, except when suction through the NBD is performed. Further, the follow-up of leak closure can also be made indirectly by observing drainage from the intracystic drain or tube, and by collapsing the cystic cavity during ultrasonography or tomography. When performing ES it is unnecessary to remove anything; rather than placing an NBD preoperatively and making the patient uncomfortable, ES can be used as an effective alternative. In our series, we observed that ES did not effectively prevent biliary leakage in only 3 patients. Moreover, as mentioned above, Ozaslan et al. (2) suggest that the most logical advantage of NBD is the introduction of the catheter above the defect. Yet, this is not always possible, and CBC may occur at the terminal branches of the biliary tract. In such a

Table 2. Summary of cases that underwent preoperative ERCP.

		Preoperative ERCP (26 patients)
Age		35.6 years (range: 12-67 years)
Number of cysts		32 (20 patients with 1 cyst, 6 patients with 2 cysts)
Cyst size		8.3 ± 4.1 cm (range: 3-16 cm), 20 cysts sized > 10 cm
Cyst Location	Right lobe	22 cysts
	Left lobe	10 cysts
Cannulation success		100% (in 4 patients after the second attempt)
CBD diameter		6-38 mm
ERCP findings	No positive findings	4 patients
	Compression of the biliary tract	2 patients
	cystic contents, germinative membranes, and purulent material in the CBD	20 patients
Success of ERCP/ES		2 patients with cholangitis underwent emergency surgery, 3 patients had postoperative biliary fistulae

Table 3. Summary of results of ERCP for postoperative biliary leakage.

		ERCP for postoperative biliary leakage (99 patients)
Number of cysts (cysts)		119 (83 patients had 1 cyst, 12 patients had 2 cysts, 4 patients had 3 cysts)
Cyst size		8.6 ± 6.1 cm
Cyst Location	Right lobe	18 cysts
	Left lobe	101 cysts
Mean amount of daily drainage		475 ± 215 cc (range: 80-1400 cc)
Cannulation success		100%
CBD diameter		14.2 ± 5.4 mm (range: 6-28 mm)
ERCP findings	No positive findings	13 patients
	Choledocholithiasis	1 patient
	CBC	79 patients
	cystic contents, germinative membranes, and purulent material in the CBD	85 patients
Success of ERCP/ES		94.9%, (21 patients required a second and 9 a third ERCP/ES)
Decrease of biliary drainage after ERCP		2.4 days (range: 1- 18 days)
End of biliary drainage after ERCP		5.2 days (range: 2-57 days).

situation, an NBD can occlude the biliary tract. Based on our study results, we conclude that the real advantages of an NBD are in placing it preoperatively for the detection of small CBCs, using it for fistulae at the level of large biliary ducts, and when fistulae do not respond to ES.

Stenting of the CBD for the treatment of biliary fistulae was suggested by Akcakaya et al. (38). They reported that biliary stenting is far superior to ES in reducing CBD pressure. It has also been reported that stenting will bypass the sphincter mechanism, which in turn will advance fistula closure (50). Akcakaya et al. (38) further reported that in 14 cases stenting during the initial procedure decreased the fistula closure time and increased the efficiency of ERCP. They also reported that the reasons for failure were

either incomplete evacuation of the CBD, or obstruction caused by residual hydatid material or unobserved stones (38). Bilsel et al. (27) placed stents in 9 of their patients for the treatment of the biliary. They stated that stenting is costly and may require repeat ERCP for removal (27). Along with the costs and the need for repeat ERCP, additional disadvantages of stenting include stent displacement and stricture formation (27). While we have not implemented the use of stents, it can be noted that in cases of overt CBC placement of a stent may be preferred as an adjunctive therapy to ES (in chronic and high output fistulae). Moreover, stents can be used in patients with CBD narrowing due to various issues (stricture formation, external compression). Stents are used to provide a bridge over the ruptured

biliary mucosa and to provide epithelization. In their experimental study concerning the comparison of stenting and ES in cystic duct leaks, Marks et al. reported that stenting more effectively reduces the time to resolution of cystic duct leaks (51); however, it is not the same as in hydatid disease because in hydatid disease the main problem is obstruction of the CBD with cystic contents. In contrast to post-cholecystectomy fistulae, which close rapidly after ES, and occasionally even close spontaneously, hydatid fistulae are more resistant and rarely close spontaneously without decompression of the biliary tract (27). Thus, it is logical to use stents when there is gross communication between the cyst and the bile duct, especially when the duct is of a large diameter; but, when communication exists at the level of the terminal branches, stents are not useful and, furthermore, can act as an obstruction. Moreover, stents have to be changed after a period of time and may also contribute to stricture formation in the biliary tract. There is also need for repeat ERCP to remove stents. Sharma et al. (43) reported that NBDs and biliary stenting were equally effective in promoting the healing of fistulae (43).

We preferred to use ES in all of our patients, as ES was effective in resolving symptoms in most of our patients. We conclude, therefore, that there is no need for stenting or NBD insertion. Mean fistula closure time was 5.2 days (range: 2-57 days) in the present study. This time has been reported to range from 2 days to 43 days (21,26,27,29,44,47-49,52). Factors influencing fistula closure were defined as time of the ERCP, cyst diameter, and fistula output. Four important factors in fistula healing are as follows: the volume of bile produced by the biliary system above the fistula, the size of the fistula, outflow pressure, and the obstructive effects of the remaining hydatid material or daughter cysts in the biliary tract (26,28).

Tekant et al. (49) reported that fistulae resolved within 7 days; the present series had a longer resolution time when compared with Tekant et al.'s results (49). In contrast to Tekant et al. (49) most of our patients underwent ERCP and ES for persistent postoperative external biliary fistulae due to HHD. Tekant et al. (49) reported that the fistulae in 10 of 11 patients that underwent ES resolved completely within 7 days.

There is no existing guideline regarding the timing of endoscopic intervention. The timing of intervention varies from a few days to several months after surgery. Since persistent external biliary fistulae are defined as those that persist after the tenth postoperative day, it is logical that ERCP should be performed after the tenth postoperative day. For our purposes, we decided to wait until after the diagnosis of a persistent fistula was confirmed before choosing immediate endoscopic intervention (21,44,47,48,52). Tekant et al. (49) reported a negative correlation between fistula closure time (duration of the fistula) and time elapsed until ERCP; therefore, they recommend early ERCP and ES. Dolay et al. (48) reported that the fistulae in their series closed within 1 month, within a median period of 10 days. They did not find any correlations between the duration of the fistulae, and their daily output and the duration of the fistulae before ERCP (48). Dolay et al. (48) further suggest that during the early postoperative period spontaneous closure will not take place in cases with high fistula output, and so early ERCP and ES should be performed. Nonetheless, they do not provide a definition of high fistula output (48). In the present study the decision to perform ERCP was made by the surgeon. There were patients in whom the procedure was performed both early and late. Similar to the findings reported by Tekant et al. (49), statistical analysis in the present study revealed a negative correlation between fistula closure time (duration of the fistula) and the time to ERCP. We observed that a shortened timeframe to endoscopic intervention correlated with a short fistula closure time.

We evaluated the relationship between the size of the cysts causing postoperative biliary fistulae, and daily fistula output and closure time. There was a positive correlation between cyst size and closure time ( $P = 0.04$ ,  $r = 0.4$ ), but there was not a correlation between cyst size and daily bile output ( $P < 0.05$ ). Interestingly, there was a positive correlation between daily output and duration of closure time ( $P = 0.01$ ,  $r = 0.04$ ).

In conclusion, we propose that ERCP and ES should be the first choice of treatment for both the pre- and postoperative biliary complications of HHD (Figure 7). Preoperative use of ERCP and ES can provide relief of symptoms, but hydatid lesions cannot

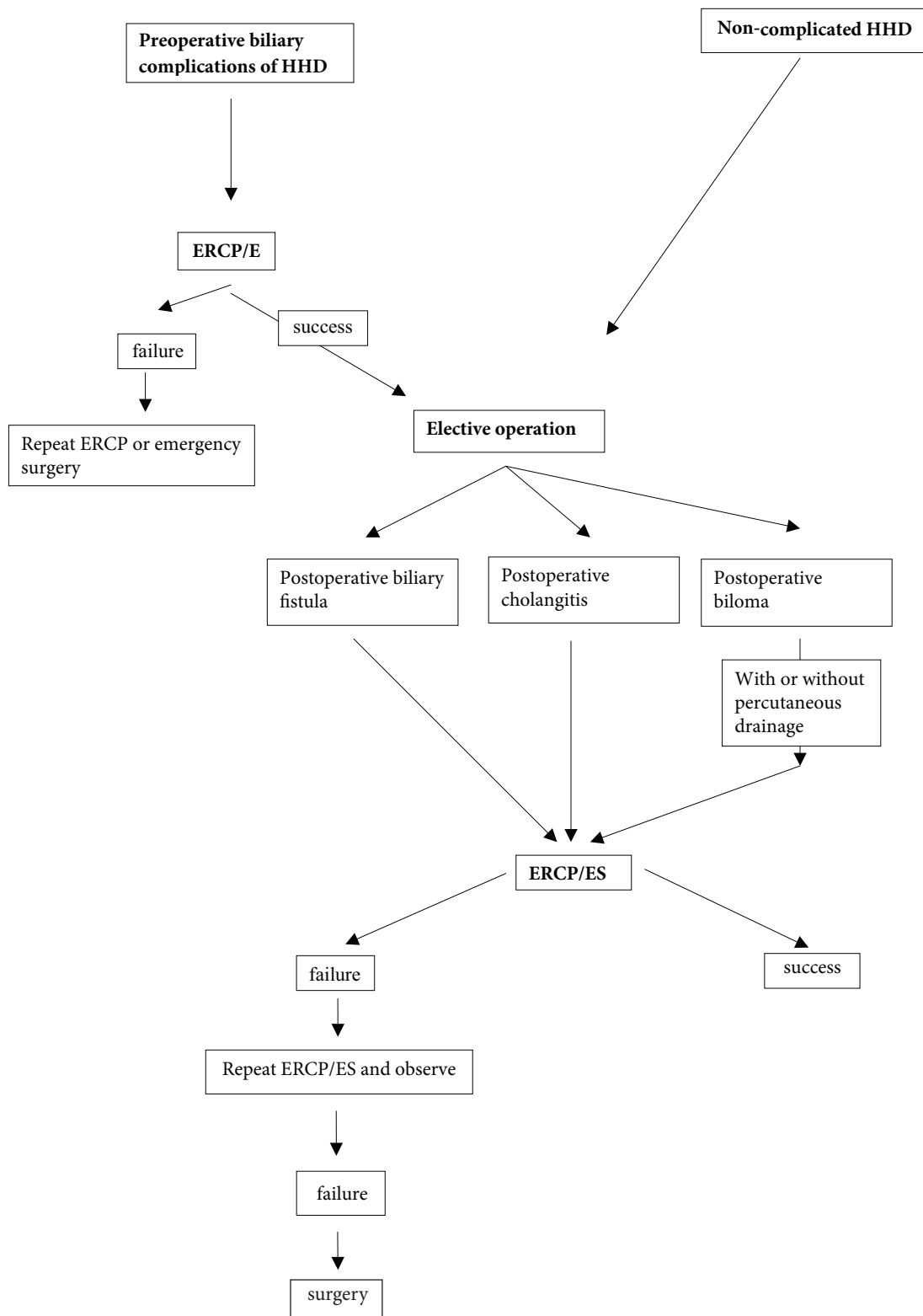


Figure 7. The proposed algorithm for the treatment of the biliary complications of HHD, based on our clinical experience.

be treated without surgery. For postoperative cholangitis and bilomas, ERCP and ES are effective. In regard to bilomas specifically, combined treatment with percutaneous drainage should be used. The success rate of ERCP and ES for postoperative biliary fistulae is high, although repeat ERCP is sometimes necessary. After performing the first endoscopic

intervention, a “wait and observe” period is necessary. NBDs and stents can be used for large defects at the level of large biliary ducts, but should not be used as a first-line treatment because of their potential disadvantages. Surgery should be the last choice for the treatment of postoperative biliary leaks after surgery for HHD.

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