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**Endoscopic or percutaneous biliary drainage in hilar cholangiocarcinoma: When and how?**

Mocan T *et al*. Biliary drainage in hilar cholangiocarcinoma

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**Abstract**

Hilar cholangiocarcinoma (hCCA) is a primary liver tumor associated with a dim prognosis. The role of preoperative and palliative biliary drainage has long been debated. The most common techniques are endoscopic retrograde cholangiopancreatography (ERCP) and percutaneous transhepatic biliary drainage (PTBD); however, recently developed endoscopic ultrasound-assisted methods are gaining more atention. Selecting the best available method in any specific scenario is crucial, yet sometimes challenging. Thus, this review aimed to discuss the available techniques, indications, perks, pitfalls, and timing-related issues in the management of hCCA. In a preoperative setting, PTBD appears to have some advantages: low risk of postprocedural complications (namely cholangitis) and better priming for surgery. For palliative purposes, we propose ERCP/PTBD depending on the experience of the operators, but also on other factors: the level of bilirubin (if very high, rather PTBD), length of the stenosis and the presence of cholangitis (PTBD), ERCP failure, or altered biliary anatomy.

**Key Words:** Hilar cholangiocarcinoma; Endoscopic biliary drainage; Percutaneous biliary drainage; Endoscopic ultrasound biliary drainage; Surgical oncology

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**Core Tip:** Hilar cholangiocarcinoma (hCCA) is a primary tumor of the liver with dim prognosis. The role of biliary drainage in curative and palliative setting has long been debated. Endoscopic retrograde cholangiopancreatography (ERCP) and percutaneous transhepatic biliary drainage (PTBD) as the most commonly used techniques. This review will highlight the available techniques, their indication, advantages or drawbacks, and also timing in the management of hCCA. In a preoperative setting, PTBD appears to win the argument as there is a lower risk of postprocedural complications and better priming for surgery. For palliative purposes, we propose ERCP/PTBD depending on the experience of the operators, biological and anatomy factors, and the presence of cholangitis.

**INTRODUCTION**

Cholangiocarcinoma (CCA) is, by definition, a primary tumor of the biliary duct system. Although it is relatively rare compared to the other hepatobiliary tumors, its burden is disproportionately high due to its typically dim prognosis. Per available reports, CCA amounts for approximately 20% of hepatobiliary tumors[1] and is the second most common primary hepatobiliary tumor, accounting for up to 25% of cases in some geographical areas[2,3]. The current gold standard for treatment is surgical resection, yet only a small portion of the patients are optimal surgery candidates. Moreover, the current standard of care is less than ideal, since the five-year recurrence-free survival for radical resection barely exceeds 33% according to the most optimistic reports[4-6].

Based on its anatomic location, CCA is classified as intra- and extrahepatic, the latter accounting for up to 90% of cases. Extrahepatic CCA is further classified as either hilar CCA (hCCA), accounting for approximately two-thirds of cases and, distal CCA amassing up to 30%[6]. As the focus of our current work, hCCA is located between the emergence of the left and right hepatic ducts and the junction between the common hepatic and the cystic ducts[7].

Due to its origin and characteristics, hCCA obstructs the hepatic bile flow, leading to painless jaundice as the main clinical staple, as it occurs in 90% of cases at diagnosis.

Furthermore, accompanying systemic manifestations such as anorexia, weight loss, and fatigue are commonplace at diagnosis, affecting more than half of the patients and rendering a poor outcome due to their association with advanced or metastatic disease[7].

Depending on initial staging, patients with hCCA are typically dichotomized into the following therapeutic pathways: curative-intent surgery or palliative care.

Either path, however, must cross the same common roadblock — addressing obstructive jaundice and reestablishing adequate bile flow. At this point, the clinician might face multiple dilemmas with regards to the benefit, timing, and method of biliary drainage. The main approaches to biliary decompression are endoscopic and percutaneous. The endoscopic approach most commonly consists of bile duct stenting *via* endoscopic retrograde cholangiopancreatography (ERCP) and, to a smaller extent, endoscopic ultrasound (EUS)-assisted methods. The percutaneous approach typically consists of ultrasound or radiological-guided transhepatic tube drainage.

In the curative-intent setting, the jury is out on whether pre-operative drainage adds a practical benefit concerning major outcomes. However, the empirical argument appears to be straightforward, as the biliary obstruction is associated with an increased risk of liver failure and cholangitis.

In the palliative setting, the role of biliary drainage can range from allowing a patient to benefit from systemic therapy with an impact on survival, to treating and preventing cholangitis, alleviating symptoms, and, not least, reducing social stigma by resolving jaundice.

The current review aims to chart a course in the field of biliary drainage of hCCA, based on the most recently available data. In the following parts, the discussion will focus on the available techniques, their indications, advantages, potential drawbacks, and timing, to further clarify the role of endoscopic and percutaneous drainage in the therapeutic arsenal of hCCA.

**ENDOSCOPIC DRAINAGE**

Most patients with obstructive jaundice due to hCCA can be managed non-surgically using ERCP. Although it is less invasive compared to the percutaneous approach, selective endoscopic stenting is technically difficult and can cause severe infectious complications, such as cholangitis. Current guidelines recommend palliative drainage of malignant hilar strictures through ERCP for Bismuth types I and II, and percutaneous transhepatic biliary drainage (PTBD) or a combination of PTBD and ERCP for Bismuth types III and IV[8].

***Plastic stents vs self-expanding metal stents***

Plastic biliary stents come in various shapes and sizes. They are made either of polyethylene, polyurethane, or Teflon. Their diameter can range from 5F to 12F, while their length ranges between 1 and 18 cm. Furthermore, there are numerous configurations available. Pigtail stents are coiled at one (single pigtail) or both ends (double pigtail), with side holes placed along the curved ends. Flanged stents may be straight, angled, or curved. They have a single flap proximally and distally with a side hole or 4 flaps without side holes[9].

Self-expanding metal stents (SEMS) are made of different metal alloys, such as nickel and titanium. They range from 4 cm to 12 cm in length and 6 mm to 10 mm in diameter when fully expanded. Biliary metallic stents can be fully covered, partially covered, or uncovered, depending on the presence or absence of a polyurethane or silicone layer.

All plastic and metal stents are radiopaque. Most SEMS models have additional proximal and distal markers, with flared ends to prevent migration[9]. Biliary stent placement is performed under radiologic guidance. Regardless of stent type, the first step is to endoscopically locatethe papilla, followed by the selective catheterization of the biliary tree. Biliary sphincterotomy is not always mandatory, as stenting without prior sphincterotomy doesn’t appear to increase the incidence of post-ERCP pancreatitis[10]. Subsequently, the bile ducts are visualized using a contrast agent, which allows the characterization of the location and extent of the stenosis. The length of the stent must be carefully selected to exceed the proximal end of the stenosis.

For plastic stents, a radiopaque guidewire is placed into the intrahepatic bile ducts. The stent is then advanced over a catheter (which acts as a pusher), which is itself placed over the guidewire. Once the stent has been adequately positioned, the catheter and guidewire are withdrawn, and the stent remains in place.

Metal stents are compressed by an outer, introducer sheath. After the desired position is achieved *via* the guidewire, the outer sheath is withdrawn, allowing the stent to expand. The guidewire is subsequently removed.

The main goal of endoscopic stenting is to drain at least 50% of the liver, which would reduce bilirubin levels by at least 50% in patients with normal liver function[11]. Secondly, cost-effectiveness must be taken into account, as well as ensuring the stent patency for as long as possible. Given these considerations, plastic stents and SEMS have been compared in several studies and meta-analyses. SEMS are associated with longer patency [odds ratio (OR) 0.16; 95% confidence interval (CI): 0.04-0.62], lower therapeutic failure (OR 0.43; 95%CI: 0.27-0.67) occlusion (OR 0.28; 95%CI: 0.19-0.39) and re-intervention rates (mean difference, -0.49; 95%CI: -0.8 to -0.19)[12-16].

SEMS are more expensive than plastic stents. However, given the higher occlusion rates in plastic stents which impose hospitalization and performing ERCP, SEMS seem to be more cost-effective in the long run[17].

Even if the diameter of fully-expanded SEMS is larger than that of plastic stents, ensuring longer patency, they are thinner when preloaded in their delivery system (5.4-8.5 Fr)[18]. Therefore, they are easier to maneuver and pass through tight strictures than their plastic counterpart. Also, SEMS’ delivery system has a sharp tip that acts as a dilatator, facilitating passage through the strictures. Uncovered SEMS also allow the drainage of the biliary tree, side branches, as opposed to plastic stents. This is especially important when performing unilateral drainage in the case of Bismuth type III-IV hilar strictures.

Taking these into account, plastic stents are no longer considered standard of care in Bismuth III-IV type CCA, but they can still be used in Bismuth type I-II[8].

***Unilateral vs bilateral stenting***

Endoscopic drainage in the case of Bismuth type I-II hilar strictures is in many ways similar to distal biliary strictures, namely patients can be fully drained with a single stent, either plastic or SEMS. However, in the case of Bismuth type III-IV malignant hilar strictures, unilateral and bilateral drainage using SEMS have been compared in several randomized control trials (RCT) and meta-analyses. In one meta-analysis that included 683 patients, side by side metal stenting (*n* = 317) yielded better clinical success rates (CSRs) (OR: 3.56; 95%CI: 1.62-7.82, *P* = 0.002) and a reduced incidence of stent dysfunction (OR: 1.74; 95%CI: 1.16-2.61, *P* = 0.007) compared to unilateral stenting (*n* = 366). Complication rates seemed to be lower in the unilateral group, although they did not reach statistical significance (OR: 0.51; 95%CI: 0.30-1.00, *P* = 0.05)[19].

In contrast, another recent meta-analysis which included a total of 21 studies with 1292 patients demonstrated that unilateral and bilateral stenting are comparable in terms of efficacy and safety, although technical success was significantly higher in the unilateral group (*P* = 0.003). One of the limitations of this meta-analysis was that the authors were unable to perform subgroup analysis based on etiology or Bismuth classification[20].

Similarly, a multicenter international study of 187 patients showed that unilateral and bilateral drainage had comparable CSR irrespective of the Bismuth classification, but with a higher incidence of complications and deaths in the bilateral group (11.7% *vs* 0%, *P* = 0.007)[21].

Bilateral drainage with SEMS is technically difficult and should be reserved for patients where placing a unilateral stent does not ensure drainage of at least 50% of the liver. Injection of a contrast agent into a liver segment that cannot be subsequently drained can lead to infectious complications such as cholangitis and the formation of liver abscesses, which negatively affect patient survival rates. For this reason, pre-interventional hepatobiliary imaging using computed tomography (CT) or magnetic resonance imaging (MRI) with the calculation of liver volume is paramount.

***Stent-in-stent vs side-by-side stent placement***

If bilateral stenting is chosen, either stent-in-stent (SIS) or stent-by-stent (SBS) drainage can be used, depending on the endoscopist’s experience and preference. However, the left lobe, right anterior, or right posterior biliary tree should be selected based on pre-interventional CT or MRI imaging to ensure the best drainage. Atrophied liver secondary to longstanding biliary obstruction or portal vein thrombosis should be avoided[22].

In the case of SBS stent placement, after catheterization of the common bile duct (CBD), two guidewires are advanced in the left and right hepatic ducts. The first stent is then advanced on the corresponding guidewire, with the recommendation that it should be placed in the hepatic duct where access is more difficult. The second stent is then advanced parallel to the first on the second guidewire as quickly as possible. The stents must be placed so that their distal ends are at the same level in the CBD or should cross the papilla, which will facilitate subsequent access if revision is necessary.

For SIS deployment, similarly to SBS deployment, two guidewires are inserted into both intrahepatic ducts bilaterally. The first stent is then inserted and deployed into the left or right intrahepatic duct. Subsequently, the guidewire used to deploy the first stent is retracted and passed through the central part of the deployed stent into the contralateral bile duct. The second stent is then advanced and deployed through the central portion of the wire mesh of the first stent. As is the case with SBS stenting, the branch that is more difficult for guidewire insertion should be selected as the first stent placement target.

When performing SIS placement, one thing to consider is that not all SEMS have the same structure. Wire mesh can be either small closed-cell or large open-cell, the latter being easier to dilate as it is weaker in its central part[18]. Hence, using an open-cell SEMS might allow an easier SIS placement.

Regarding their efficacy, one prospective (*n* = 69) and one retrospective (*n* = 64) study showed that SIS and SBS deployment seem to be similar in terms of clinical success, stent patency and adverse events[22,23] . In addition, a meta-analysis of four studies which included 158 patients in total revealed no significant differences with respect to the rates of successful placement (*P* = 0.799), successful drainage (*P* = 0.617), early complications (*P* = 0.738), late complications (*P* = 0.744) and stent occlusions (*P* = 0.606)[24].

***Complications of endoscopic stenting***

A common complication of stent placement is duodenal biliary reflux, with secondary bacterial colonization of the biliary tract and sludge/stone formation. Another complication is related to stent deployment too far inside the duodenum, or its migration, with subsequent impaction of the stent flanges in the duodenal wall and perforation. If stents migrate in the bowel they can also become stuck, mostly in the ileocecal valve, leading to bowel obstruction.

Plastic stent dysfunction is managed by stent removal and replacement either with another plastic stent or a SEMS. In the case of SEMS dysfunction, if the occlusion is due to debris, this can be removed using balloon catheters. If the occlusion is caused by tissue ingrowth or overgrowth, a secondary plastic stent or SEMS can be inserted inside the existing stent.

**IS THERE ANY ROOM FOR EUS-GUIDED BILIARY DRAINAGE IN THE MANAGEMENT OF HCCA?**

Although ERCP and PTBD are the two established biliary decompression techniques in the management of hCCA, EUS-guided biliary drainage (EUS-BD) has gained more and more interest in the gastroenterology community[25]. In theory, EUD-BD seems to provide multiple advantages to the management of hCCA, since it does not require the passage of the biliary stricture. However, in clinical practice, it appears to only be used when ERCP has failed, in surgically altered anatomy, or failed re-interventions for blockage of transpapillary placed stents[26]. Although scarce, the most common adverse effects associated with EUS-BD are bleeding, peritonitis, pneumoperitoneum, cholangitis, bile leak, and stent migration[27]. Moreover, its limitations also reside in the insufficient number of expert endosonographers, typically found only in tertiary referral centers.

The types of EUS-BD performed in malignant hilar obstruction are: (1) EUS-guided hepato-gastrostomy (EUS-HGS); (2) Bridging therapies; and (3) EUS-guided hepatico-duodenostomy (EUS-HDS).

EUS-HGS is one of the most commonly used EUS-BD procedures *via* an intrahepatic approach[27]. Technically, the EUS-HGS procedure drains only the left hepatic lobe, leaving the right biliary system undrained and thus increases the risk of potential life-threatening cholangitis.

To address this caveat, Ogura *et al*[28] developed a novel technique of EUS-BD for right intrahepatic biliary obstruction by adding an uncovered metal stent to the EUS-HGS to bridge the obstruction. In brief, after catheterizing the biliary tract *via* the stomach and reaching the left liver lobe using a 19-gauge fine-needle aspiration and a guidewire, the needle is replaced by a standard catheter, a guidewire is passed through the hilar stricture and into the right hepatic biliary system. Functional success was reported in all patients and no severe adverse events were noted. Dismally, the bridging method is technically very challenging when passing the guidewire to the right intrahepatic biliary system and requires trained experts.

Last but not least, the right intrahepatic biliary channels could be accessed by EUS-HDS in a similar manner to EUS-HGS, the only variation being the approach *via* the duodenum. However, since the technique is performed on the lateral side of the duodenal bulb or proximal second duodenum, a long endoscope position might be unstable and risky. For this reason, its use is very limited in the management of hCCA[29,30].

To date, there are several studies carried out to evaluate the use of EUS-BD in clinical practice. Unfortunately, the majority used EUS-BD as a salvation technique (leading to an important selection bias) and the number of patients involved is small[28,31-33]. Nevertheless, there are some advantages of EUS-BD that could make it a more beneficial procedure in the future. The combination of ERCP and EUS-BD (CERES) appears to be more appealing than PTBD in the treatment of Bismuth III-IV CCA. In 2021, Kongkam *et al*[34] reported a similar technical success rate (TSR), CSR and complications rate (CR) of CERES *vs* PTBD as follows: TSR = 84.2% (16/19) *vs* 100% (17/17) (*P* = 0.23), CSR = 78.9% (15/19) *vs* 76.5% (13/17) (*P* = 1), and CR = 26.3 (5/19) *vs* 35.3 (6/17) (*P* = 0.56), respectively. Moreover, regarding recurrent biliary obstruction within 3 and 6 mo, authors reported improved results of the CERES procedure[34]. Several retrospective and prospective studies comparing EUS-BD *vs* PTBD in malignant distal obstruction favor EUS-BD as a better tool for biliary drainage[35,36]. Moreover, a multicenter survey evaluating patient preference for either EUS-BD or PTBD has shown that more than 80% of patients preferred EUS-BD, citing an increased quality of life without the discomfort of an external drain tube (78.1%), a higher success rate with relatively lower morbidity (43.8%) and the opportunity to be performed at the same time as ERCP (28.3%)[37]. However, no study compared EUS drainage with PTBD in patients with hCCA. While certainly promising, limited experience and low availability diminish the use of EUS-BD. To this point, there is insufficient data to suggest that EUS-BD can replace PTBD as a more efficient biliary drainage tool, with current applicability in large centers with vast EUS experience.

**PTBD AND PERCUTANEOUS BILIARY STENTING**

PTBD can be performed in two clinical scenarios: (1) Before surgery to relieve biliary obstruction and subsequent cholestasis since an improved survival was documented[38,39]; and (2) As a palliative technique with the ultimate goal to decrease the bilirubin levels to a level that can allow chemotherapy.

Compared to endoscopic drainage, the use of the PTBD method has the advantage that a specific duct can be easily targeted to maximize the drainage of functional parenchyma[40-42].In high bile duct obstruction, right and left hepatic ducts are typically isolated, with no distal communication. There are three types of isolation: (1) Complete: Cholangiography doesn’t result in any opacification; (2) Effective: Isolated ducts are opacified but they do not drain; and (3) Impending isolation: The biliary duct is opacified and drains, but has a central narrowing that is likely to progress to complete isolation. This is important as the latter two increase the risk of subsequent cholangitis.

The first (and probably the most important) steps when assessing a patient for PTBD are: (1) To evaluate the viability of liver parenchyma by high-quality CT or MRI (*e.g.*, drainage of a portion of the liver without an intact portal venous blood supply with ipsilateral duct obstruction will not result in the improvement of liver function; and (2) Pre-procedural antibiotic prophylaxis as cholangitis could result in serious complications that could delay or complicate further management.

***Types of PTBD***

Currently, there are three modalities of PTBD: (1) External biliary drainage; (2) Internal-external biliary drainage; and (3) Percutaneous self-expanding metallic stent placement.

The point of access is typically chosen depending on the location of the stenosis and the type of intervention. Typically, the right-sided access may be preferred for stent placement in high obstruction, as it offers anatomical continuity between the right hepatic duct and the CBD. When the obstruction is below the duct bifurcation, a left approach is advisable due to a lower risk of catheter displacement. When ascites or segmental isolation of the right duct are present, a left-sided approach may provide more benefit. Peripheral access is preferred because of the lower risk of bleeding and inadequate drainage.

There are two types of approaches: Fluoroscopy-guided PTBD (F-PTBD) and a combined ultrasound-guided approach (US-PTBD). The US-PTBD has more advantages: reduction of fluoroscopy time, faster access to the bile ducts, reduced number of punctures, and, consequently, significantly lowers rates of complications. Moreover, a meta-analysis showed the superiority of US-PTBD *vs* F-PTBD, as US-PTBD was associated with fewer severe early complications and procedure-related deaths (overall complication rates range from 5%-100% for F-PTBD (median, 21%) and from 0%-22% for US-PTBD (median, 5%)[43,44]. After localizing the best access pathway, the real-time US-guided puncture of the liver parenchyma is performed with a 21-gauge Chiba needle. In the case of F-PTBD, after injecting the contrast agent, the targeted bile duct is accessed *via* fluoroscopy. Afterward, the inner stylet is withdrawn, and a guidewire is inserted through the needle into the collecting system.

Subsequently, progressive 6, 8, and 10 Fr coaxial sheaths are advanced over the guidewire for tract dilation, and ultimately an 8 Fr or 10 Fr biliary drainage catheter is placed. If the obstruction can be passed, the directional catheter is advanced into the small bowel. The catheter can be then exchanged over a stiffer wire for a multisidehole drainage catheter. This allows the bile to drain both externally (into a bag), and internally (into the duodenum) to preserve the normal enterohepatic circulation of bile.

Finally, a percutaneous SEMS is a third option for drainage. Stent placement can be performed as either a one-step (primary stenting technique) or a two-step (secondary stenting technique) procedure; the latter will give the clinician more time to plan and is particularly useful in case of intraprocedural bleeding. A randomized controlled trial that compared the clinical effectiveness of percutaneous covered Viabil stents *vs* uncovered metallic Wallstents demonstrated improved survival in patients with hCCA who received a covered (median survival, 243 d) *vs* uncovered stent (median survival, 180 d) (*P* = 0.039). The incidence of stent dysfunction was significantly lower in the covered stent group[45].

***Post transhepatic percutaneous biliary drainage complications***

Virtually, PTBD complications are overlapped to those of endoscopic biliary drainage, hence we won’t reiterate the matter. However, in the group of patients with resectable hCCA, a long-term complication that can be a game~~-~~changer is represented by tumor seeding. Takahashi and colleagues reported an alarming 5.2 percent catheter tract recurrence after PTBD in patients with hCCA which is much higher than previously reported. However, the duration of PTBD (over 60 d) was an important independent risk factor for tract metastasis and shortened postoperative survival. In the curative surgery setting, this points out the importance of a shortdelay until surgery to prevent this troublesome complication[46,47].

***Combined techniques — “Rendez-vous”: how and when?***

Rendez-vous (RV) procedure is an appealing option for treating obstructive jaundice in the case of an unsuccessful ERCP[48-50]. Apart from ERCP failure, RV is a rescue therapy for in the case of complex biliary interventions that require combined access routes: patients with surgically altered enteric anatomy, tight hilar biliary stricture passable only by the guidewire, and in patients with a preexistent PTBD that can be easily used as an anterograde route for percutaneous RV[50,51].

***Clinical scenarios: Single or dual drainage?***

In the case of distal biliary obstruction, a straightforward approach is sufficient. However, in the case of Bismuth type II, III, IV hCCA controversy exists as to whether partial or total biliary drainage is more suitable in a palliative setting. There are two majors advocates for complete[52] or incomplete[53] drainage.

Schima *et al*[54] studied a group of 41 patients with hilar obstruction and compared long-term outcomes. Single stents were placed for unilateral drainage in 27 patients, while 14 patients had bilateral stents. They found no significant difference regarding mean stent patency.

Kaiho *et al*[55] performed either complete (*n* = 12) or partial (*n* = 9) drainage in a group of 21 patients with hilar obstruction. There were three, seven, and eleven patients with Bismuth types II, III, and IV obstructions, respectively. They found no difference in stent patency between complete and partial drainage.

Inal *et al*[56] evaluated the necessity of draining more than one hepatic duct in 138 patients with malignant hilar obstruction. Single-duct drainage was achieved in 74 patients (54%) by placing one stent (*n* = 59), two stents (*n* = 41) or a single transhepatic tract in a “T” configuration (*n* = 23). There were no differences between single and dual stenting in Bismuth type I, II, and III hCCA. However, in Bismuth type IV, the deployment of two parallel stents resulted in significantly higher patency rates.

Lee *et al*[57] suggest that when a repeat procedure in proximal hCCA is necessary, placement of internal/external drainage catheters provides better palliation than putting in new metal stents, as life expectancy is limited in this patient group.

**ENDOSCOPIC *VS* PERCUTANEOUS BILIARY DRAINAGE — PRO AND CONS**

After decades of clinical research, it is still unclear whether endoscopic (ERCP) or percutaneous drainage is the preferred method of biliary drainage in patients with hCCA. Both can be performed before surgery (in patients suited for curative treatment) or as a palliative treatment. Choosing one technique over the other is not an easy clinical decision. A straightforward selection can only be made in patients with modified anatomy[58].

However, for the majority of patients with hCCA choosing the best technique depends on several factors.

***Biliary drainage before surgery***

In one retrospective study, technical success in the ERCP group (*n* = 87) was 78% compared to 98% in the PTBD group (*n* = 42; *P* = 0.04). The therapeutic success rate was also higher in the PTBD group (79% *vs* 49%; *P* = 0.02)[59]. Another retrospective study showed higher technical success for PTBD versus ERCP (100 % *vs* 81%; *P* = 0.203)[60]. However, neither technical nor therapeutic success should be the sole primary outcomes when comparing the two methods. There is only one multicentric RCT comparing endoscopic and percutaneous biliary drainage. The primary outcome was the number of severe complications in the timespan between randomization and surgery. In total, 54 patients were randomly assigned to benefit from either PTBD or ERCP. The study was prematurely interrupted due to significantly higher mortality in the PTBD group [11 (41%) of 27 patients] *vs* the ERCP group [three (11%) of 27 patients; relative risk 3.67, 95%CI 1.15-11.69; *P* = 0.03][61]. Indeed this study provides the highest level of evidence we have to this point for decision making in clinical practice. However, these data should be interpreted with caution for several reasons: (1) Only one patient with Bismuth type 1 was included in the PTBD group; (2) Although not statistically significant, both technical and therapeutic success were higher in the PTBD group; (3) 55% of the patients in the ERCP group had subsequent PTBD; and (4) Only 54 patients were randomized, making the study prone to a type-I error. Nevertheless, the expertise of centers performing PTBD is highly relevant and could explain these results. In one study[62], low-volume centers showed a higher occurrence of serious complications related to PTBD, whereas high-volume centers showed a similar proportion of complications between endoscopic and percutaneous drainage. In terms of procedure-related complications (*e.g.*, cholangitis and pancreatitis) two other studies found PTBD to be superior to ERCP[63,64]. Another critical aspect is the cost associated with each method. One recent study found ERCP to be more expensive than PTBD (*P* = 0.005)[63]. Some patients with hCCA are better suited for ERCP drainage, while others might be more appropriate for PTBD. Discriminating between these two categories is crucial. One study showed that patients with Bismuth 3a or 4 hCCA and a total bilirubin level above 8.8 mg/dL should be considered for initial PTBD rather than ERCP[65].

ERCP appears to perform better in Bismuth II hCCA, as it is associated with fewer postprocedural complications, namely cholangitis[66].

Until now, four meta-analyses comparing the two techniques have been published[67-70]. All of them found PTBD to be superior to some extent over ERCP. More data about the meta-analyses is provided in Table 1.

***Biliary drainage in palliation***

A single meta-analysis comparing ERCP and PTBD in palliation of advanced malignant hilar obstruction has been published to this point. It included a total of nine studies and 546 patients, yet not all of them had hCCA. The results showed that palliation with PTBD was associated with higher rates of successful biliary drainage and lower rates of cholangitis while palliative ERCP had lower bleeding complications[71].

A key aspect in a palliative setting is the patient’s quality of life. In this light, the presence of the external drainage tube for the remainder of a patient’s life (in the case of PTBD) might generate a significant alteration, especially compared to the placement of an internal stent. Surprisingly, based on a controlled study by Saluja *et al*[72]*,* quality of life after PTBD was rated higher than ERCP according to the World Health Organization Quality of Life physical and psychological scores at one and three months. A potential cause might be the relatively high incidence rate of fever in the endoscopic biliary stent implementation group. Moreover, percutaneous stenting after PTBD is also possible, eliminating the burden of caring for an external drainage tube for the entire life. One study which included 85 patients with advanced Bismuth type III and IV hCCA showed that percutaneous SEMS was superior to endoscopic stenting regarding successful biliary decompression (92.7% *vs* 77.3%; *P* = 0.49)[73]. There is not enough evidence to suggest one technique over the other. Moreover, the implementation of RCTs is problematic. The results of an unsuccessful RCT were recently published. Lack of funding, provider/institutional bias in favor of one procedure, and logistical challenges were cited as possible responsible factors of failure[74]. Therefore, until high-quality observational data or RCTs become available, one must rely on personal judgment, according to expertise and specific conditions. Based on the aforementioned discussion, we propose an algorithm on when and how to use ERCP and PTBD in patients with hCCA, depicted in Figure 1.

**THE SURGICAL POINT OF VIEW**

Biliary drainage is an established safe hCCA treatment strategy as a bridge therapy before surgery. To date, the surgical standard of treatment in hCCA is complete resection combined surgery. Although there is debate about the effect of biliary drainage on surgical outcomes in patients with hCCA, it has been demonstrated that liver failure caused by obstructive jaundice can be a significant risk factor in major liver resection. This is especially relevant in the case of hCCA, for which extended hepatectomy might be needed to provide the best chance for a cure. Therefore, it is preferable to perform the biliary decompression of the future remnant liver to preserve postoperative liver function[75].

There are two preferred methods for biliary drainage in hCCA: Endoscopic biliary drainage (ERCP) and PTBD. ERCP might be a less invasive technique, but it may come with a price: it carries an increased risk of ascending cholangitis and procedure-related complications, such as duodenal perforation and pancreatitis[59-60,64,67,76]. On the other hand, PTBD could lead to several complications such as bleeding, portal vein thrombosis, tumor seeding, patient discomfort, and has been widely reported to be associated with malpractice[64,77-80].

Several meta-analyses have compared the two methods in hCCA patients[67-70]. All of them showed some superiority of PTBD over ERCP when performed before surgery.

In our center, as surgeons, we always prefer PTBD drainage over endoscopic drainage. From our own experience several other factors must be taken into account: (1) First, the cornerstone of surgical treatment is to obtain an R0 resection, which translates in performing an accurate dissection of the hepatic pedicle and lymph node dissection. This is significantly easier in the absence of inflammation surrounding the main biliary duct (MBD), which might be caused by a prior ERCP[81], resulting in greater intraoperative blood loss and prolonged operative time; (2) In the case of PTBD, inflammation is absent or minimal, which leads to an easier dissection and an accurate lymph node dissection[82]; and (3) The inflammation determined by the stent could give a false appreciation of inoperability[83]. The inflammation surrounding the MBD can be a blunder in mimicking a direct invasion of the important vascular structures, such as the portal vein or the hepatic artery, which would falsely classify the patient as inoperable. Consequently, with ERCP, we consider that the best timing for surgery is within the first seven days, to avoid MBD inflammation. A concern is that the seven-day timeline could not suffice to obtain a normal liver function, a problem that doesn’t exist for PTBD.

**CONCLUSION**

Endoscopic or percutaneous biliary drainage? Decades of experience, a lot of research, new stents, new techniques but the same disease: hCCA remains one of the most challenging cancers. Biliary drainage, then chemotherapy, stent occlusion/external tube removal then stop chemotherapy and re-drain, and the story goes on. Treating patients according to the proposed algorithm (Figure 1), although based on low-quality data and personal experience and educated guesses might at least help the decision-making process. In the palliative setting, we would choose between ERCP and PTBD generally based on operator experience, as well as other relevant factors: stenosis length, bilirubin level (if very high, rather PTBD), cholangitis (PTBD), ERCP failure, or altered biliary anatomy. Not least, one should always consider patient preference It is not hard to understand that (from the patient perspective) there is only one answer to the question: endoscopic or percutaneous biliary drainage? EUS biliary drainage is a relatively new technique with only a few hCCA patients treated. Yet it is likely to gain more interest in the years to come, hoping to improve the current management of hCCA.

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**Footnotes**

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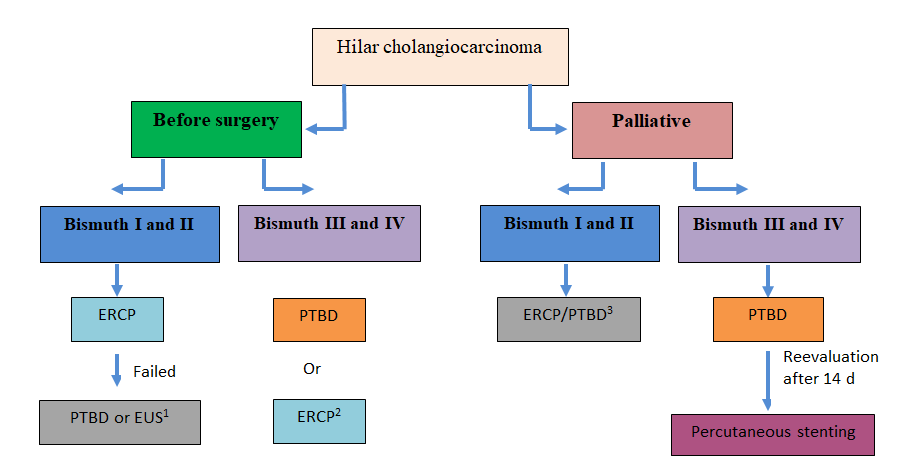
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**Figure Legends**



**Figure 1 Management algorithm in hilar cholangiocarcinoma.** 1In high-volume centers with expertise in EUS. 2In centers specialized in ERCP and little experience in PTBD. 3Depending on the experience and preference of the patient. ERCP: Endoscopic retrograde cholangio-pancreatography; EUS: Endoscopic ultrasound; PTBD: Percutaneous transhepatic biliary drainage.

**Table 1 Meta-analysis comparing endoscopic versus biliary drainage before surgery in patients with hilar cholangiocarcinoma**

|  |  |  |  |
| --- | --- | --- | --- |
| **Ref.** | **No studies** | **No. patients** | **Main findings** |
| Liu *et al*[68] | 6 | 359-EBD; 286-PTBD | Similar technical success rate, R0 resection, incidence of total complications after resection, post-operative hospitalization time, resection time and recurrence; The incidence of total complications were higher in the EBD group (*P* < 0.05) |
| Hameed *et al*[69] | 15 | 398-EBD; 1036-PTBD | There was a trend towards higher procedure conversion (RR 7.36, *P* = 0.07) and cholangitis (RR 3.36, *P* = 0.15) in the EBD group |
| Al Mahjoub *et al*[70] | 4 | 275-EBD; 158-PTBD | Overall procedure related mortality was higher in EBD group (*P* = 0.0009); Similar initial technical failure; Conversion rate was higher in EBD group (*P* < 0.001); Risk of pancreatitis was higher in EBD group (*P* < 0.001); Risk of cholangitis was higher in EBD group (*P* < 0.001); Similar postoperative morbidity and mortality |
| Tang *et al*[67] | 9 | 498-EBD; 414-PTBD | PTBD was associated with a lower risk of cholangitis (*P* < 0.001); PTBD was associated with a lower risk of pancreatitis (*P* = 0.003); A higher successful rate of palliative relief of cholestasis in PTBD group (*P* < 0.001); The incidence of hemorrhage was similar (*P* = 0.59) |

EBD: Endoscopic biliary drainage; PTBD: Percutaneous biliary drainage; hCCA: Hilar cholangiocarcinoma; RR: Relative risk.