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The role of endoscopy in malignant hilar obstruction

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Abstract

Malignant hilar biliary obstruction (MHO) is a medical challenge as regards both forming a correct diagnosis and its adequate management, in terms of treatment alternatives and palliative options. Surgical resection is the only curative treatment for the underlying disease, but the majority of patients are not suitable candidates because of an unresectable tumor or poor performance status. Biliary drainage (BD) can be achieved through the percutaneous transhepatic route or endoscopically, and the choice depends on a host of factors, including biliary anatomy and comorbidity of the patient. Though there is no consensus, the endoscopic approach is usually preferred over the former. Endoscopy can aid in both diagnosis (collection of histological as well as cytological samples, direct visualization of suspected malignant pathology, or use of endoscopic ultrasound [EUS] for evaluation and locoregional staging), and in achieving internal BD. Advances in the development of various stents, accessories and, more recently, the use of EUS have in fact further expanded its application in MHO management. The choice of stents to be used (type, make, and number), palliation methods, deployment techniques and the use of local ablative strategy are still evolving and require more data. The complexity of management of MHO mandates that each patient should receive a "personalized approach", all the way from establishing a diagnosis until final treatment, with the help of a multidisciplinary team effort. Herein, we provide a comprehensive literature review of the current role of endoscopy for MHO, according to its applications in various clinical settings.

Keywords Biliary obstruction, endoscopic retrograde cholangiopancreatography, endoscopic ultrasound, cholangiocarcinoma, cholangioscopy

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Introduction

Malignant hilar biliary obstruction (MHO) is a complex disease in terms of its anatomy, difficulty of early diagnosis and management options. The most common cause of a malignant hilar stricture is hilar cholangiocarcinoma (CCA) [1,2]. Other etiologies include gallbladder carcinoma, hepatocellular carcinoma, lymphomas, and metastatic disease from other malignancies. Pathologically, CCA is locally aggressive and tends to spread along the ductal wall, infiltrating the adjacent structures [3]; morphologically the tumors are predominantly scirrhous/sclerotic in nature. Consequently, tissue diagnosis using biopsy or cytology becomes difficult [4]. While the curative therapy is surgery, tumors often present late, and even then only 20-40% of the potentially operable ones are offered surgical resection [5]. Thus, the majority of patients require palliative BD for the obstructive jaundice or the intense pruritus.

The anatomic involvement of the biliary system, apart from its histological character, is another key feature that governs the management options. The Bismuth-Corlette classification system is used to classify MHO into 4 categories. Bismuth type I is when the stricture involves the main duct, sparing the primary confluence; type II involves the confluence; type III involves the confluence and one of the sectorial confluences, sparing the contralateral one—IIIa for the right sectorial involvement and IIIb for the left; and type IV involves both the right and left sectorial confluences together [6]. The higher the grade of obstruction, the more

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extensive the tumor volume and the more complex the anatomy, precluding optimum BD.

The role of endoscopy in MHO extends from establishing the diagnosis to managing its consequences, such as relief of obstructive jaundice or cholangitis, as well as palliation. The endoscopic armamentarium has expanded. Apart from conventional endoscopic retrograde cholangiopancreatography (ERCP), newer technologies—such as cholangioscopy and guided biopsy, endoscopic ultrasound (EUS)-guided tissue diagnosis and BD, photodynamic therapy (PDT), radiofrequency ablation (RFA), etc.—have widened the scope of endoscopy. In this review, we aim to provide an overview of the present role of endoscopy for diagnosis, the various therapeutic options available for the management of MHO, and the concept of a "tailor-made' treatment for tackling the complex anatomy of these strictures.

Literature search

A search was performed in PubMed and Embase using the search strategy outlined in Supplementary Document 1. All studies were reviewed, including case reports, series, clinical studies and reviews related to the role of endoscopy in MHO, both diagnostic and therapeutic. The use of ERCP and EUS in distal biliary obstruction is beyond the scope of this review.

Diagnostic approach in MHO

The main approach in the management of hilar stricture is to differentiate between benign and malignant etiologies and then assess resectability. A dedicated cross-sectional imaging examination—multidetector computed tomography (MDCT) scan or magnetic resonance imaging (MRI) with magnetic resonance cholangiopancreatography (MRCP)—is imperative to get the initial roadmap (Fig. 1). These modalities are complementary: while computed tomography (CT) helps provide information on locoregional staging, metastasis and vascular involvement, MRCP delineates the intraductal extension [7]. The role of endoscopy in the diagnosis of MHO is primarily to provide cytological or histological samples. EUS and other advanced imaging techniques, such as cholangioscopy, confocal laser endomicroscopy or intraductal ultrasound, can further increase the diagnostic yield.

The following modalities are useful in the diagnosis of MHO:

I. ERCP

ERCP is now a therapeutic procedure, but a cholangiogram revealing a long irregular, asymmetric stricture is more consistent with a malignant cause of hilar block. During ERCP, several diagnostic tools can be used to obtain cytological/tissue samples.

A. Biliary brush cytology: This is routinely performed, easy to use but has low sensitivity (20-40%) and high specificity (90-100%) [8]. Use of a greater number of brushing passes (>30) has recently been shown to increase diagnostic yield (57% vs. 38%) when compared to 10 passes [9]. Stricture dilatation pre-procedure does not improve the sensitivity of biliary brushings (34.5% vs. 31%) [10].

B. Intraductal biopsy forceps: This provides a more complete tissue sample (inclusion of subepithelial stroma) but is more complex (sensitivity 48%, specificity 99%). A meta-analysis comparing brushing to forceps biopsy suggested the combination of both only increased sensitivity modestly, to 59.4% [11].

C. Newer add-on techniques: Liquid-based cytology has been shown to have higher sensitivity (78% vs. 56%) and accuracy (88.3% vs. 66.5%) than conventional smears [12]. Similarly, the endoscopic scraper (with cell-block) has shown better yield than biliary cytology [13]. Fluorescence *in-situ* hybridization and flow-cytometry have been recommended as an adjunct, especially in cases with normal cytology and a suspicious malignant stricture [14].

II. Cholangioscopy

This allows direct visualization of the biliary mucosa and can be used to perform targeted biopsies. A meta-analysis reported high sensitivity (94%) and specificity (95%) for diagnosis of indeterminate biliary strictures. Spyglass cholangioscopy can provide a diagnosis in up to 82% cases with prior inconclusive brushing, and has an accuracy of 89% [15] (Fig. 1). The Monaco classification has been proposed: it uses 8 visual criteria for malignant biliary lesions (presence of stricture, lesion type, mucosal features, papillary projections, ulcers, abnormal vessels, scarring, and pit-pattern) to increase diagnostic accuracy [16].

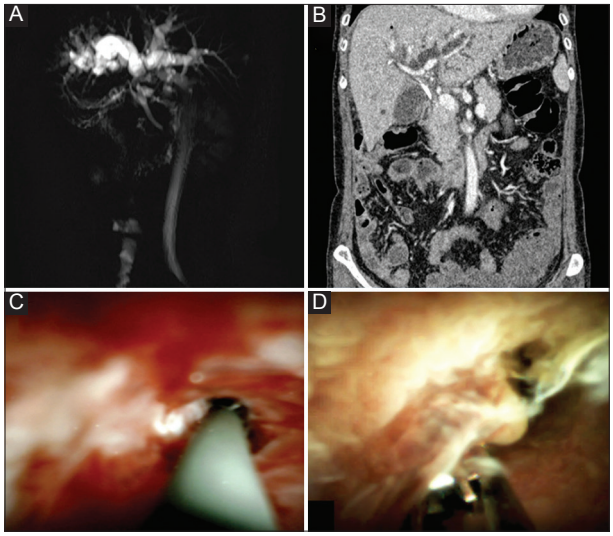

Figure 1 Diagnostic workup for malignant hilar obstruction: (A) reconstruction image of magnetic resonance cholangiopancreatography depicting type II hilar obstruction; (B) coronal reconstruction computed tomography image showing hilar obstruction; (C) Cholangioscopy image showing malignant stricture; (D) cholangioscopy-guided biopsy from papillary projections of cholangiocarcinoma (*Image courtesy: Dr Saurabh Mukewar, Midas Hospital, Nagpur, India*)

III. EUS

The armamentarium of EUS has rapidly expanded for both diagnostic and therapeutic interventions for MHO. It helps in tumor visualization and locoregional staging. EUS-guided fine-needle aspiration, followed by biopsy (EUS-FNA/B), has been shown to be helpful in ERCP-negative strictures, especially when combined with ERCP-guided biopsy in the same session [17,18]. It is a safe procedure, with minimal risk of needle tract tumor seeding. The usefulness of EUS-FNA/B depends on the location of the malignant stricture. Sadeghi *et al* reported that the pooled sensitivity of EUS-FNA was higher for distal malignant strictures than for hilar (83% vs. 76%) [19]. It is generally recommended to perform cholangioscopy-guided biopsy for MHO (accuracy 93.6%) and EUS-FNA/B for distal malignant strictures (96.3%) [20].

IV. Newer diagnostic modalities

Various newer modalities have been utilized alongside ERCP to increase diagnostic sensitivity. Intraductal ultrasound (IDUS) consists of a tiny probe inserted inside bile ducts to evaluate the wall architecture. ERCP+IDUS has been shown to be superior to EUS for strictures of uncertain etiology (accuracy 91% vs. 74%) [21]. Similarly, intraductal confocal laser endomicroscopy (CLE) and optical coherence tomography (OCT) are available for direct bile duct visualization. CLE has higher sensitivity (88% vs. 54%) than ERCP-guided sampling for biliary strictures [22]. Very few studies exist on the use of OCT for characterization of malignancy [23]. These new modalities act as adjuncts in cases involving ERCP/EUS/cholangioscopy-negative biliary strictures. Their role is not well defined and their use is limited by the high cost.

Treatment of MHO

I. Points to be evaluated prior to therapeutic management of MHO:

A. Biliary anatomy: The aim of draining the biliary system is to achieve "effective BD (EBD)". This is defined as a reduction in bilirubin by more than 50% of baseline at 2 weeks, and/or bilirubin <3.0 mg/dL at 4 weeks after endoscopic drainage. It is prudent to understand the anatomy of the biliary system, and the volume of liver segments to be drained, before embarking on the decision regarding the optimum drainage strategy (percutaneous vs. endoscopic) for managing MHO [24]. As highlighted earlier, proper cross-sectional imaging is a prerequisite to establish a "road-map" for determining the best route of drainage. The use of 3D reconstruction additionally helps in collecting data for assessing vascular anatomy, hepatic parenchymal involvement, metastasis and biliary tree encasement [7]. It helps to identify which liver segments are to be drained (to avoid post-procedure cholangitis) and which additional procedures must consequently be performed, such as portal vein (PV) embolization (PVE) in the case of segmental parenchymal atrophy [25].

Criteria for unresectability of hilar CCA are well established [26]. Studies have shown that CT has the highest pooled sensitivity (95%), closely followed by MRI (94%), in assessing the resectability of hilar CCA [7]. The left hepatic duct (LHD) (1.7 cm long, 3 mm diameter) is more superficial and runs a straighter course, draining segments 2, 3 and 4, while the right hepatic duct (RHD) is shorter (0.9 cm long, 2.6 mm diameter), and divides earlier than the left, into 2 segments, anterior (draining segment V, VIII) and posterior (draining segment VI, VII). As a result, the RHD is more prone to tumoral obstruction than the LHD. Understanding the normal biliary anatomy and then determining the Bismuth classification is important before deciding on the management algorithm, more so if multi-segmental drainage is needed [6,27].

B. Draining the "optimal" liver volume: The clinical goal of BD is to prolong survival and improve the quality of life (QoL), without any increase in adverse events (AEs). Drainage of "optimal liver volume" governs the effectiveness of any BD procedure and is considered physiologically ideal. The RHD, LHD and caudate lobe drain 55-60%, 30-35% and 10% of liver volume, respectively [27]. An initial study by Dowsett *et al* recommended drainage of 25% of liver volume to achieve EBD [28]. But lately, to achieve improved survival, it has been suggested that 50% of liver volume should be drained, as highlighted by Vienne *et al* (survival 119 vs. 59 days, P=0.005) [29]. Similarly, Takahashi *et al* have given a cutoff of 33% for patients with preserved liver function, and 50% for patients with impaired liver function, to achieve EBD [30]. The major impediment in achieving 50% liver volume drainage occurs in high-grade strictures (Bismuth III/IV). Hence, if a single stent or system drainage cannot achieve the desired results, then bilateral or multi-sectoral drainage should be considered [31].

C. Level of experience of the endoscopist: Endoscopic stenting of MHO is a complex procedure, graded with a difficulty level of 3 as per the recommendations of the American Society for Gastrointestinal Endoscopy (ASGE). This implies that the rate of technical failure with AEs is quite high [32]. Endoscopic management of a high-grade hilar stricture requires a more experienced endoscopist. Studies have shown that low-volume centers (<87 ERCPs/year), low-level endoscopist experience (<25 ERCPs/year) and degree of difficulty were independent predictors of adverse outcomes [33]. Nowadays, with advancements in ERCP/EUS techniques, palliation of MHO has shown outstanding results. Thus, the ASGE guideline recommends that the choice between percutaneous transhepatic BD (PTBD) and endoscopy (ERCP/EUS) should be based on patient preferences, disease characteristics, and local expertise [34].

II. Preoperative BD (PBD)

In resectable cases the use of PBD is not routinely recommended. Since the morbidity and mortality following surgery are high in jaundiced patients, the use of PBD may be advocated, balancing the risks and benefits for each patient. One of the definite indications for PBD is low future liver remnant (FLR) volume (<30%). Low FLR results in a high risk of postoperative liver failure and mortality. In such cases, PVE is required to achieve remnant liver hypertrophy and PBD decreases the risk of hepatic insufficiency [35]. Other indications include cholangitis, intractable pruritus, hyperbilirubinemia-induced malnutrition, hepatic or renal insufficiency, prior to neo-adjuvant therapy, and in cases of delay in surgery [36].

A. PBD vs. no-PBD: There has been no randomized trial that compared PBD vs. no-PBD in MHO—unlike distal malignant obstruction, where PBD has been shown to increase the risk of serious complications compared to direct surgery (74% vs. 34%, P<0.001) [37]. Several retrospective studies have shown more post-surgical infectious complications without a survival benefit (40% vs. 17%). It has been proposed that this is a result of a shift in biliary microbiome, facilitating the spread of aggressive resistant bacteria [38]. Thus, PBD should be attempted only for specific indications.

B. Method of preoperative BD (ERCP vs. PTBD): Comparative studies on endoscopic vs. PTBD for MHO show conflicting results. Two meta-analyses have shown that PTBD has a lower risk of cholangitis, particularly in Bismuth III/IV, compared to endoscopic drainage [39,40]. In contrast, the only randomized controlled trial (RCT) comparing the 2 approaches was prematurely terminated because of the higher mortality in the PTBD group (41% vs. 11%, P=0.03) [41]. Similarly, Kishi *et al* reported higher postoperative morbidity after PTBD (23% vs. 3%) [42], with a higher risk of peritoneal metastasis (odds ratio [OR] 6.9, 95% confidence interval [CI] 1.9-25.7; P=0.004). Among the endoscopic techniques, few studies have favored placement of a nasobiliary drain (NBD) over endoscopic stenting and PTBD [43]. However, NBD entails prolonged hospitalization, risk of self-removal, and patient discomfort, limiting its widespread use.

C. Optimal duration and pre-operative bilirubin levels for PBD: Following PBD, it takes 4-8 weeks for complete resolution of jaundice, which in turn translates to better recovery of hepatic function. But postponing surgery after PBD for >2 weeks has been shown to be associated with bacterial translocation and tumor dissemination. A preoperative bilirubin level >3 mg/dL has shown to be a negative predictor of overall survival [44]. Thus, PBD just prior to surgery with a target bilirubin <3 mg/dL seems ideal.

Overall, PBD may be indicated for the reasons highlighted above. Endoscopic drainage seems to be an equally effective but safer alternative to PTBD, as it allows a more physiological internal drainage. However, the final route depends on local expertise and on the ductal anatomy. Prophylactic antibiotics are mandatory. ASGE guidelines advise against the routine use of PTBD as first-line therapy in patients with MHO undergoing PBD [34], although, more studies including RCTs are needed to substantiate this.

III. Strategies for optimal palliative BD in MHO

A. What to choose for palliation of MHO: ERCP vs. PTBD? Based on the initial literature search, PTBD was considered to be superior to endoscopy for palliative BD in patients with MHO, because of its greater technical feasibility, durability and similar AEs. Paik *et al* showed better technical success (TS) of percutaneous self-expandable metal stents (SEMS) than endoscopic SEMS (92.7% vs. 77.3%, P=0.049) for high-grade hilar CCA, with similar complications, stent patency and survival [45].

However, PTBD has its own set of limitations: a) the presence of an external catheter leads to pain and discomfort, and diminishes QoL; b) external bile drainage is not physiological; c) it is technically difficult in the case of ascites, liver metastasis, coagulopathy or a non-dilated biliary system; and d) tube dislodgement or peri-catheter leak, necessitating multiple reinterventions.

Hence, endoscopic palliation is now being increasingly preferred for its convenience (physiological drainage) and improved QoL. Furthermore, with the expanding armamentarium of stents, guidewires (GWs), accessories and alternate access options, such as EUS-BD, endoscopic management has shown higher TS and clinical success (CS) rates with similar stent patency, even for advanced MHO.

Though the Asia-Pacific and European Society of Gastrointestinal Endoscopy (ESGE) guidelines have preferred PTBD for advanced MHO, the latest ASGE guidelines suggest that the decisions about palliative drainage depends on patient preference, local expertise and underlying disease characteristics [25,31,34]. Nevertheless, ERCP and PTBD are not competing modalities, but rather play complementary roles.

B. Endoscopic drainage: plastic vs. metal stents: Plastic stents (PS) are the most commonly used stents for BD in MHO, irrespective of the level or severity of block. They are relatively cheap, and are easy to exchange or remove in case of malfunction. Because of their moldability and ability to adapt to the singular biliary tree, they are recommended in PBD, as they do not hamper subsequent therapies, such as ablation or surgery. Their main drawback is stent migration (5.3%) and stent occlusion (up to 30%) [46]. Among PS, theoretically, double-pigtail stents (DPT-PS) tend to have lower distal migration rates as a result of the anchorage provided by the pigtail loop, but a recent retrospective study comparing DPT vs. straight PS reported that the latter had lower migration rates (27.4% vs. 17.3%, respectively; P=0.002) [47]. Hence, PS are associated with higher reintervention rates, greater cost and inferior QoL (Fig. 2).

On the other hand, SEMS have a larger diameter, which translates into higher patency, lower reintervention and better

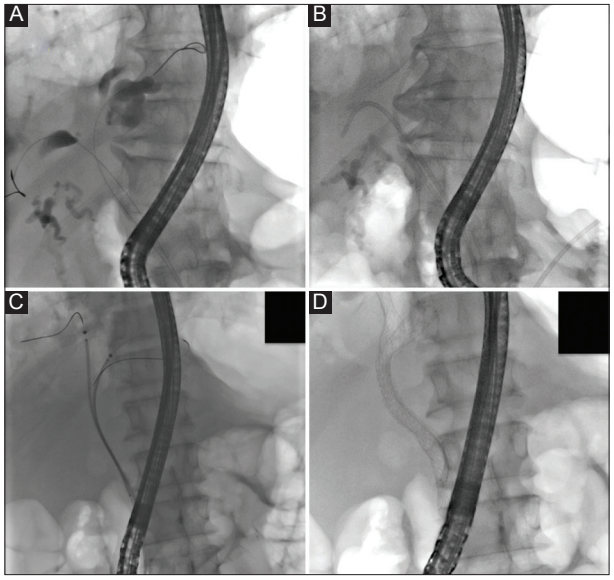

Figure 2 Endoscopic retrograde cholangiopancreatography for malignant hilar obstruction: (A) fluoroscopic image of wire negotiated into both systems; (B) plastic stents placed in both systems; (C) fluoroscopic image of simultaneous side-by-side placement of delivery catheter of metal stent (Epic™, Boston Scientific, USA); (D) Bilateral metal stents deployed

cost-effectiveness. Uncovered SEMS (U-SEMS) are usually recommended for palliation of MHO. Their open mesh design does not occlude the cystic duct or side-branches of intrahepatic ducts (IHD), thus reducing post-procedure cholangitis. The thinner delivery system (5.4-8.5 Fr) with tapered tip and rigid catheter, facilitates easy passage through tight strictures, which is difficult when PS are being deployed.

Multiple studies (including 3 RCTs) have compared SEMS vs. PS and found the former to be better in terms of higher stent patency, lower reintervention and similar survival rates [48-56] (Table 1). A meta-analysis by Sawas *et al* reported lower occlusion rates of SEMS vs. PS in MHO (OR 0.28, 95%CI 0.19-0.39) [57].

The main drawback of U-SEMS is stent occlusion by tumor ingrowth, sludge, food debris or blood clots, which occurs in about 20-50% of cases [48-53]. Embedded stents can be difficult to remove after malfunction and stent revision is more difficult than PS. Covered-SEMS (C-SEMS) have a thin flexible outer membrane that prevents tumor ingrowth. However, C-SEMS are difficult to deploy in hilar blocks and can be occluded by biofilm formation, with the added disadvantages of stent migration and side-branch occlusion. Thus, guidelines suggest the use of U-SEMS for palliation of high-grade MHO, especially in patients with a life expectancy >3 months [25,31,34].

C. Unilateral vs. bilateral drainage: Multiple studies have investigated the role of unilateral vs. bilateral drainage for MHO. The volume of liver drained translates into EBD. Unilateral stenting is technically easier, with reportedly lower AEs. An initial study by Polydorou *et al* reported similar CS with similar complications and survival rates [74]. Subsequently, an RCT by De Palma *et al* reported higher TS (88.6% vs. 76.9%, P=0.041) with lower AEs (18.9% vs. 26.9%, P=0.026) in the unilateral stent group [59].

However, an emerging concept that has been shown to improve survival is drainage of >50% of liver volume [29]. Unilateral stents are faced with an issue of incomplete drainage, more so in high-grade hilar blocks. Hence, guidelines recommend placement of multiple stents (bilateral or multi-segmental) to achieve >50% liver volume drainage in advanced MHO [25,34]. This is particularly helpful when both hepatic lobes are diseased or bilateral ablation therapy is planned. Nonetheless, placing multiple stents increases the technical complexity of the procedure. Inadvertent contrast injection during endoscopy and later failure to achieve BD may lead to post-procedure cholangitis and reduced survival. This can be avoided by using 3D-CT/MRCP prior to the procedure, with proper image analysis, and the procedure should be performed by an experienced endoscopist at a high-volume center [60].

Chang *et al* first reported the benefits of bilateral stenting in MHO. The overall median survival was higher in the bilateral drainage group (131 vs. 62 days) [61]. An RCT by Lee *et al* reported similar TS but lower reintervention (42.6% vs. 60.3%, P=0.04) and higher patency rates (252 vs. 139 days) in the bilateral drainage group [62]. Studies comparing unilateral vs. bilateral stenting have been tabulated in Table 2. In view of the prevailing evidence, bilateral or multi-segmental drainage with metal stents to achieve a more physiological >50% liver volume drainage is recommended in advanced MHO.

D. Opacification of ducts during drainage: contrast vs. air: Inability to achieve BD in MHO after delineating the biliary anatomy by contrast injection may lead to post-procedure cholangitis and adverse clinical outcomes. The use of air to obtain a cholangiogram has been described for facilitating successful stent insertion in cases of advanced MHO [68].

E. Endoscopic multi-segmental drainage using SEMS: technique and efficacy

1. Endoscopic bilateral stent-in-stent (SIS) vs. stent-by-stent (SBS) deployment

Advanced MHO requires multi-segmental drainage to achieve a more physiological >50% liver volume drainage. Commonly, two techniques are available for bilateral stenting: SBS and SIS.

i. SBS technique: This refers to sequential or simultaneous placement of 2 SEMS [69,70]. The 2 GWs are passed initially into the intended IHD planned for drainage; subsequently, the stents are deployed one after the other over the GW in a side-to-side manner. Simultaneous placement of SEMS is now possible using a smaller 6-Fr stent delivery system (Zilver 635, Cook Medical, Winston-Salem, NC, USA; Epic, Boston Scientific, Natick, MA, USA) with a therapeutic duodenoscope that has a working channel of at least 3.8 mm (Fig. 2) [71].

ii. SIS technique: In this technique, the second stent is placed through the wire mesh of the first SEMS and a Y-shaped configuration is achieved. Large biliary sphincterotomy is not usually recommended to preserve the function of the sphincter, believed to reduce ascending cholangitis [71].

iii. Advantages and disadvantages of both techniques: Both techniques mandate the need of experienced endoscopists

Table 1 Studies comparing metal vs. plastic stents for palliative drainage in malignant hilar obstruction

Study [ref.], year	Design	SEMS vs. plastic stent (number)	Technical success (%)	Clinical success (%)	Reintervention (times/patient)	Stent patency	Adverse events (%)	Overall survival
Wagner *et al* [48], 1993	RCT	11 vs. 9	100% vs. 88.9%	NA	0.4 vs. 2.4	81.8% vs. 50% (in >30 days)	Cholangitis (9.1% vs. 33.3%)	NA
Sangchan *et al* [49], 2012	RCT	54 vs. 54	83.3% vs. 85.2%	70.4% vs. 46.3%	1.16 vs. 1.23	103 vs. 35 days	Early (25.9% vs. 40.7%); late (46.3% vs. 33.3%); cholangitis (14.8% vs. 24%)	126 vs. 49 days
Mukai *et al* [50], 2013	RCT	30 vs. 30	100% vs. 100%	NA	0.63 vs. 1.8	81% vs. 20% (at 6 months)	3% vs. 3%	219.5 vs. 188.5 days
Perdue *et al* [51], 2008	Prospective	34 vs. 28	97% vs. 85%	NA	11.8% vs. 32.1%	NA	Stent related complications (11.8% vs. 39.3%); cholangitis (5.9% vs. 10.7%)	8.8% vs. 14.3% (at 30 days)
Liberato *et al* [52], 2012	Retrospective	249 vs. 231	98.8% vs. 88.3%	97.9% vs. 84.8%	24.4% vs. 56.4%	27 vs. 20 weeks	Early (2% vs. 8.3%); late (24.4% vs. 56.4%); cholangitis (5.7% vs. 33.3%)	45 vs. 46 weeks
Raju *et al* [53], 2011	Retrospective	48 vs. 52	95.8% vs. 94.2%	NA	1.53 vs. 4.6	5.56 vs. 1.86 months	8.3% vs. 7.7%; cholangitis (2.1% vs. 3.8%)	9.08 vs. 8.22 months
Xia *et al* [44], 2020	Retrospective	Bilateral stents (111 vs. 151)	100% vs. 100%	98.9% vs. 71.4%	1.2 vs. 2	9.6 vs. 4.6 months	Cholangitis (8% vs. 26.4%) [PSM]	7.1 vs. 4.1 months
Xia *et al* [55], 2021	Retrospective	Bilateral stents (111 vs. 151); after PSM (96 vs. 96)	100% vs. 100%	99% vs. 71.9%	1.3 vs. 2	9.2 vs. 4.8 months	Cholangitis (7.3% vs. 26%)	7.2 vs. 4.1 months
Kim *et al* [56], 2021	Retrospective	Bilateral SEMS (35) vs. MPS (67)	100% vs. 100%	71.4% vs. 65.6%	40% vs. 56.7%	112 vs. 56 days	Plastic vs. metal: overall OR 1.49 (95%CI 0.52-4.23) (similar); cholangitis (HR 2.89; 95%CI 1.57-5.29; higher in MPS)	NA

RCT, randomized controlled trial; NA, not available; PSM, propensity score matching; MPS, multiple plastic stents; OR, odds ratio; HR, hazard ratio; CI, confidence interval

at high volume centers. Overall, TS of SBS and SIS ranges from 73-100% [72,73]. An RCT comparing the 2 techniques showed no difference in CS and AEs, including stent patency at 3 and 6 months [74]. Two recent meta-analyses have shown that, although SIS and SBS have comparable CS and pooled AEs, the former has higher TS and the latter has higher stent patency rates [75,76].

SIS has the following advantages: a) Y-shaped configuration is more physiological (less axial and lateral force on the common bile duct [CBD] and surrounding vasculature); and b) multi-sectoral drainage is feasible. However, SIS is technically a more difficult procedure. If stent malfunction occurs, the Y-shaped design prohibits reinsertion of the GW. SBS is technically easier, along with stent revision and GW manipulation. However, parallel deployment of 2 SEMS in the CBD can compress the adjacent PV, leading to thrombosis [77]. Other technical issues include entanglement of GW, difficulty in precise deployment of SEMS, and inadequate expansion of SEMS in case of a non-dilated CBD. In either case, stents can be deployed above or below the papilla. Stents deployed above the

Table 2 Studies comparing unilateral vs. bilateral drainage (using endoscopic guidance) for palliative drainage in malignant hilar obstruction

Study [ref.], year	Design	Unilateral vs. bilateral drainage	Technical success (n %)	Clinical success (%)	Reintervention (times/patient)	Stent patency	Adverse events (%)	Overall survival
Studies showing unilateral drainage similar/better than bilateral drainage								
De Palma *et al* [59], 2001	RCT	79 vs. 78; all plastic	88.6% vs. 76.9%	81% vs. 73%	NA	NA	Early (18.9% vs. 26.9%); late (39.7% vs. 39.1%); cholangitis (8.8% vs. 16.6%)	140 vs. 142 days
Iwano *et al* [63], 2011	Retrospective	65 vs. 17; all SEMS	95.2% vs. 89.5%	NA	NA	133 vs. 125 days (p=0.32)	Overall (36.9% vs. 41.2%); cholangitis (12.3% vs. 11.8%); liver abscess (1.5% vs. 17.6%)	170 vs. 184 days (P=0.49)
Yin *et al* [64], 2019	Retrospective	51 vs. 42; all SEMS	92.1% vs. 95.2%	95.7% vs. 97	NA	189 vs. 198 days	Overall, 6.38% vs. 12.5%	222 vs. 202 days
Teng *et al* [65], 2019	Retrospective	55 vs. 47; all SEMS	93.1% vs. 90.4%	96.4% vs. 97.9%	NA	182 vs. 198 days	Overall, 16.3% vs. 14.8%; cholangitis 11% vs. 8.5%	189 vs. 199 days
Hakuta *et al* [66], 2021	RCT	19 vs. 25; all SEMS	100% vs. 100%	NA	39% vs. 5.1%	11.1 vs. 4.3 months; (RBO 42% vs. 44%)	early (5.3% vs. 28%); cholangitis (5.3% vs. 20%); late (47% vs. 44%)	NA
Studies showing bilateral drainage is better than unilateral drainage								
Chang *et al* [61], 1998	Retrospective	For Bismuth II+III (Both metal+plastic): 29 vs. 37	NA	NA	NA	NA	Overall (38% vs. 3%)	46 vs. 225 days
Lee *et al* [62], 2017	RCT	66 vs. 67; all SEMS	100% vs. 95.5%	84.9% vs. 95.3%	60.3% vs. 42.6% (per-protocol analysis)	139 vs. 252 days	Early (27.3% vs. 6.2%); late (47% vs. 43.8%); cholangitis (9.1% vs. 4.7%)	178 vs. 270 days
Naitoh *et al* [67], 2009	Retrospective	17 vs. 29; all SEMS	100% vs. 90%	94% vs. 90%	59% vs. 23%	210 vs. 488 days	Early (0 vs. 10%); late (65% vs. 54%);	166 vs. 205 days
Xia *et al* [54], 2020	Retrospective	Propensity matched (87 vs. 97); all SEMS	NA	98.9% vs. 83.5%	1.2 vs. 1.7	9.6 vs. 6.8 months	Cholangitis (8% vs. 17.5%)	7.1 vs. 4.4 months

RCT, randomized controlled trial; NA, not available; SEMS, self-expandable metal stents; RBO, recurrent biliary obstruction

papilla can help prevent duodenal reflux but those kept below allow ease of reintervention.

SBS and SIS have similar efficacy and the choice depends on the local expertise and stent availability. Comparative

studies of the SBS and SIS techniques have been highlighted in Supplementary Table 1.

2. *Endoscopic multiple (>2) branched stenting*

Theoretically, triple drainage of the right anterior, right posterior and left duct is ideal when treating an advanced MHO. Placement of ≥3 plastic stents is still technically more feasible as compared to SEMS. It can be done using SBS, SIS, or a combination of these techniques. Kawamoto *et al* initially described a series of 9 cases treated with the SIS technique using JOSTENT SelfX stents, with 100% TS [78]. Placement of a third stent can act as a salvage procedure for early clinical failure of bilateral stenting, as described by Lee *et al* [79].

These techniques have been performed at expert high volume centers with small sample sizes. Prospective studies with larger sample sizes are needed to validate the results.

F. EUS-BD: Recent advances in the field of EUS have revolutionized the management of MHO. EUS-BD is now being increasingly used for palliation, or as a rescue option in cases of failed/non-feasible ERCP or surgically altered anatomy. Four techniques of EUS-BD have been described: EUS-guided hepaticogastrostomy (EUS-HGS), EUS-guided hepaticoduodenostomy (EUS-HDS), the bridging method and CERES (combination of ERCP and EUS-BD).

1. EUS-HGS: This involves creation of a transmural tract between the left IHD and the stomach (technical steps in Supplementary Table 2). TS and CS vary between 65-100% and 76-100%, respectively with 23% AEs [80,81] (Fig. 3).
   EUS-HGS can also be safely performed in cases with moderate-severe cholangitis. The author's center reported the use of EUS-HGS in 19 cases of MHO, with 100% TS and 78.9% CS; reintervention was necessary in 4 cases [82].
   A comparison of EUS-HGS vs. PTBD for MHO in failed ERCP cases has also been reported at the author's center. Comparative analysis showed similar CS but lower overall AEs (15.8% vs. 44.4%, P=0.04) and a shorter hospital stay (median 6 vs. 11 days, P=0.007) in the EUS-HGS arm [83].
2. EUS-HDS: First reported by Park *et al*, EUS-HDS is performed rather less frequently than EUS-HGS [84]. The largest series (35 cases, of which 71.4% were MHO), reported 97.1% TS and 80% CS [85]. Interestingly, there are isolated case reports describing the use of combined EUS-HGS and EUS-HDS in MHO [86] (Fig. 3).
3. Bridging therapy: Ogura *et al* described a technique of "bridge therapy" in cases of separated right and left IHDs [87]. Caillol *et al* reported bridge therapy in MHO, with 83% CS [88].
   A few caveats to this procedure include: a) it is a technically challenging procedure, with GW manipulation being a major impediment to TS; b) stent selection is key, and the U-SEMS with laser-cut design is considered best, to avoid side-branch occlusion and stent shortening. Reintervention is easy for both systems through the covered SEMS.
4. CERES: Combined use of EUS-BD and ERCP, known as the CERES technique, has been described recently. It is a method of primary BD in which ERCP with single SEMS is placed in either the right or left IHD, after which the other ductal system is drained using EUS-BD [89]. This technique circumvents the shortcomings of PTBD or ERCP with bilateral SEMS, allowing internal drainage and minimizing AEs.

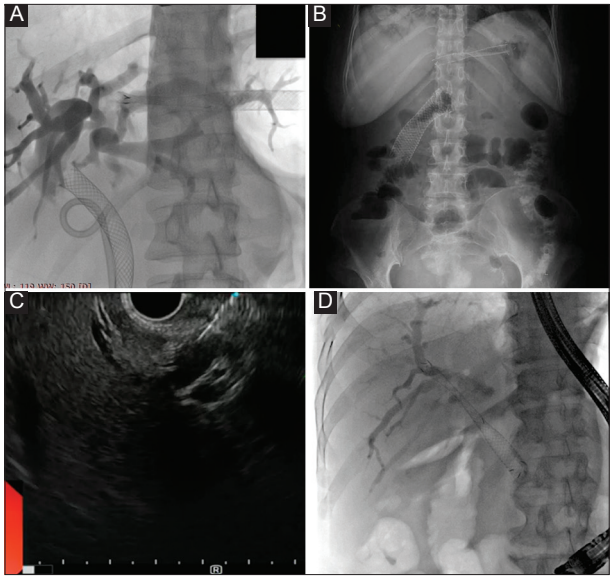

Figure 3 Endoscopic ultrasound (EUS)-guided biliary drainage for malignant hilar obstruction: (A) EUS-guided hepaticogastrostomy in a patient with previously placed transpapillary biliary metal stent for hilar obstruction; (B) EUS-guided hepaticogastrostomy for malignant hilar obstruction with gastric outlet obstruction with duodenal self-expandable metal stent *in situ*; (C) EUS image of dilated right ductal system punctured with needle; (D) EUS-guided hepatico-duodenostomy

IV. Reintervention post-endoscopic BD (ERCP or EUS-BD)
Recurrent biliary obstruction (RBO) post SEMS for MHO ranges from 3-45% [90]. It has been attributed to either tumor- or stent-related AEs. To plan an appropriate endoscopic reintervention (EnRi) strategy, the following must be considered on a case-by-case basis: urgency of BD, cause of RBO, initial BD method used, which system is left undrained, anatomy of stents within the biliary system, and available expertise. Various options depend on the stent to be used (plastic vs. metal; covered or uncovered SEMS; SBS or SIS technique used) and the BD procedure (PTBD, ERCP, EUS-BD, or combination). Regardless of the original method used, in case of hemodynamic instability, PTBD is always the first choice.

For MHO, planning an EnRi is more complex and technically challenging than distal block. Cross-sectional imaging using CT or MRCP to assess which biliary segment to target is of utmost importance.

A. EnRi for plastic stents: Exchange of original PS, "inside-PS" placement or SEMS placement [91]. Yoshida *et al* have described a novel "snare-over-GW" method for PS replacement, especially in proximal biliary stenosis [92].
B. EnRi for SEMS (placed by SIS method): Placement of new stents (PS or C-SEMS) is the only option in such cases. EnRi for SIS anatomy is technically demanding, because of the difficulty in GW negotiation. Lee *et al* reported 83.3% TS and 79.2% CS for EnRi in SIS configuration [93].

C. EnRi for SEMS (placed by SBS method): This is technically easier because of the ease of GW manipulation. Insertion of GW as a loop helps in ensuring the GW within the stent lumen rather than through the mesh. Lee *et al* reported 45% RBO rates with a success rate for EnRi of 92% [69].
D. EnRi for EUS-BD: Rates of RBO are lower in EUS-BD, as the stent does not traverse the tumor. Methods for reintervention proposed are: cutting the stent using an electrosurgical generator, placing NBD, dedicated long PS designed for EUS-HGS, placement of hemoclips to prevent stent migration, placement of 2 PS in crisscross manner at the proximal end, or placement of C-SEMS within the originally placed SEMS [80,90].

V. Local ablation strategies

In patients with advanced MHO who are unsuitable for surgical management, overall QoL, survival and stent patency can be prolonged with the help of locoregional therapy (LRT). this includes PDT, RFA, and brachytherapy (BT).

A. PDT: This involves injection of a photosensitizer (hematoporphyrin derivative) activated in the target tissue (tumor) by a laser of specific wavelength. Published research has reported endoscopic drainage with intraluminal PDT being the best palliative method to prolong stent patency. Ortner *et al*, in their RCT, reported a longer median survival in the PDT with stent vs. only stent group (493 vs. 98, P<0.0001), with similar AEs [94]. Phototoxicity is usually

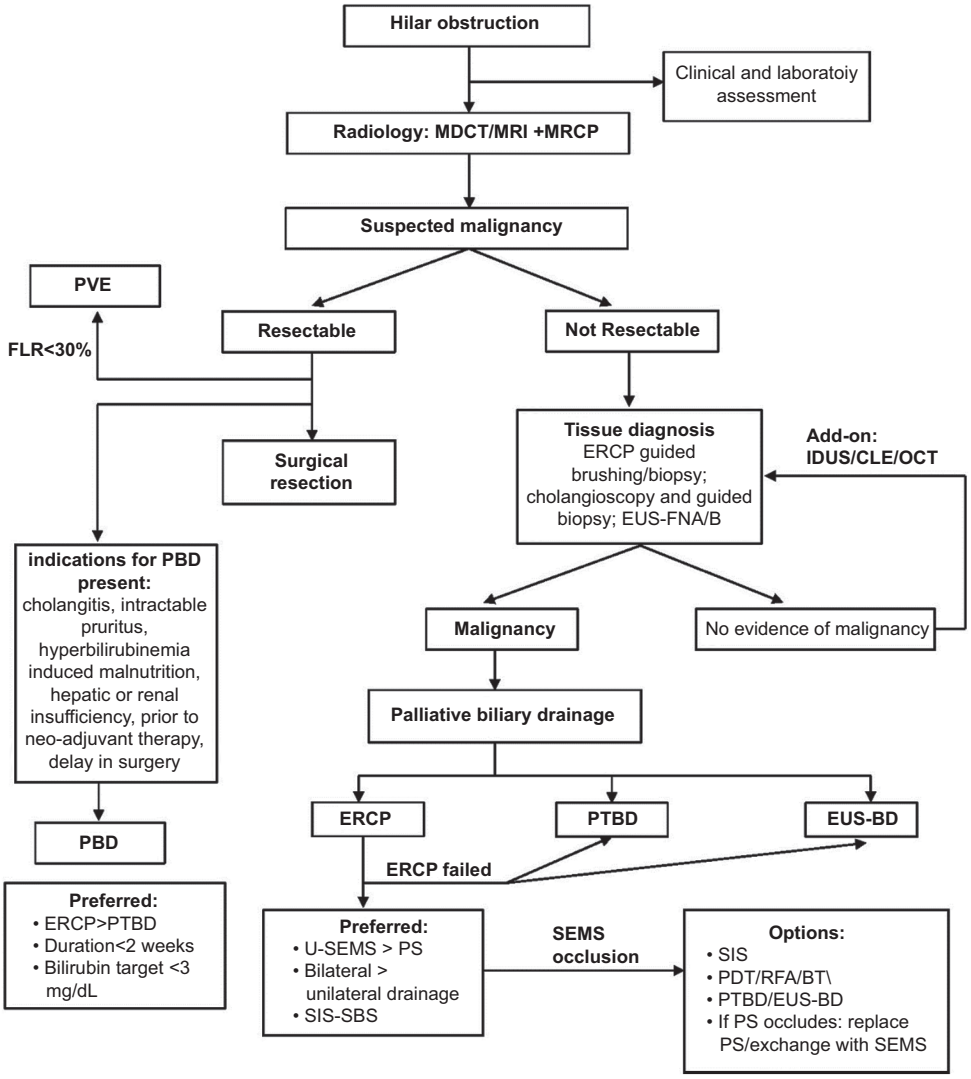

Figure 4 Algorithm for the role of endoscopy in the diagnosis and therapeutic management of malignant hilar obstruction
MDCT, multidetector computed tomography; MRI, magnetic resonance imaging; MRCP, magnetic resonance cholangiopancreatography; FLR, future liver remnant; PVE, portal vein embolization; PBD, pre-operative biliary drainage; ERCP, endoscopic retrograde cholangiopancreatography; EUS, endoscopic ultrasound; FNA/B, fine-needle aspiration/biopsy; IDUS, intraductal ultrasound; CLE, confocal laser endomicroscopy; OCT, optical coherence tomography; PTBD, percutaneous transhepatic biliary drainage; EUS-BD, EUS-guided biliary drainage; U-SEMS, uncovered self-expandable biliary stent; PS, plastic stent; SIS, stent-in-stent; SBS, stent-by-stent; PDT, photodynamic therapy; RFA, radiofrequency ablation; BT, brachytherapy

a troublesome complication in these cases (Supplementary Table 3).

B. RFA: This is local therapy that generates very high temperature within local tissue, causing tissue necrosis. It is cheaper than PDT and does not lead to phototoxicity, hence may be preferred. Intrabiliary RFA is performed using an RFA catheter during ERCP. Schmidt *et al* compared RFA vs. PDT in hilar CCA and reported that short term AEs were higher in the PDT group (40% vs. 21%), with greater number of stent exchanges (65% vs. 29%) [95]. Despite earlier studies reporting good outcomes, one recent RCT reported no additional benefit of adding RFA to SEMS in MHO (6-month stent patency 33.3% vs. 52.4%, P=0.6) [96]. Intraductal RFA has also been utilized as a rescue procedure for treating RBO by tumor ingrowth [97]. A recent meta-analysis of studies involving PDT, RFA and only-stent groups for CCA reported overall better survival in the PDT group (11.9 vs. 8.1 vs. 6.7 months) and lower 30-day mortality (3.3% vs. 7% vs. 4.9%) [98] (Supplementary Table 4).

C. BT: Isolated case reports exist on the use of BT by delivering high dose radiation to the local area, using an NBD placed within the bile duct [99].

Thus, concurrently administered LRT along with endoscopic stenting and systemic chemotherapy seems to improve stent patency and overall survival. However, ASGE guidelines have suggested that RFA/PDT through SEMS should be performed only at research institutes or tertiary care referral centers [34].

Concluding remarks

The management of MHO requires a multidisciplinary team approach to provide personalized care from diagnosis to final treatment (Fig. 4). The diagnostic algorithm mandates starting from a basic clinical and laboratory assessment. Proper cross-sectional imaging is needed prior to any intervention, to assess for anatomical involvement, staging and resectability. Surgery may be offered upfront to those fulfilling the radiological criteria of malignancy and are deemed resectable, sometimes even without a pathological diagnosis. For surgically unsuitable candidates or inoperable MHO cases, cytological or histological sampling is important. This can be obtained by ERCP-guided brush/biopsy, cholangioscopy or EUS-FNA/B.

For therapeutic management of advanced MHO, the goal of endoscopic palliation is "EBD". Physiologically, it is usually achieved with multi-segmental drainage of >50% liver volume. Preoperative BD is ideally indicated only in selected cases. With advances in endoscopic techniques, uncovered-SEMS is recommended for both PBD and palliative drainage. For multi-segmental drainage, both SIS and SBS techniques are comparable in terms of technical difficulty and efficacy, so the choice mainly depends on local expertise, stent availability, biliary anatomy and consideration for second reintervention. EUS-BD has shown promise for palliation or as a rescue option in cases of failed/non-feasible ERCP or surgically altered anatomy. Finally, to prolong stent patency and survival, local ablative treatment can be performed along with SEMS to decrease the tumor burden. The final goal of endoscopic palliation of MHO is to prolong QoL and improve stent patency and survival. Larger, prospective, multicenter studies including RCTs are needed to further substantiate the role of endoscopy in the management of MHO.

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Supplementary material

Supplementary Document 1

Search: (((malignant hilar obstruction) OR (cholangiocarcinoma)) OR (malignant biliary obstruction)) AND ((((endoscopy) OR (endotherapy)) OR (endoscopic retrograde cholangiography)) OR (endoscopic ultrasound))

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Supplementary Table 1 Comparative studies on the endoscopic deployment of stents using SBS and SIS techniques

Study [ref.], year	Design	SIS vs. SBS (sample size)	Technical success (%)	Clinical success (%)	Early adverse events (%)	Late adverse events (%)	Overall adverse events (%)	Occlusion rates (%)	Median stent patency	Median survival
Naitoh *et al* [72], 2012	Retrospective	24 vs. 28	100 vs. 89	100 vs. 96	4 vs. 11	8 vs. 32	13 vs. 44; cholangitis (4% vs. 20%)	42 vs. 20	104 vs. 155 days	159 vs. 198 days
Kim *et al* [A], 2012	Retrospective	22 vs. 19	100 vs. 100	81.8 vs. 78.9	22.7 vs. 31.6	50 vs. 36.8	72.7 vs. 68.4; cholangitis (9.1% vs. 10.5%)	59.1 vs. 47.4	134 vs. 118 days	225 vs. 146 days
Law *et al* [B], 2013	Retrospective	7 vs. 17	100 vs. 100	NA	NA	NA	Overall, 4 cases	42.9 vs. 52.9	Overall, 86 days	NA
Lee *et al* [74], 2018	RCT	34 vs. 35	100 vs. 91.4	94.1 vs. 90.6	11.8 vs. 11.4	17.6 vs. 22.9	23.5 vs. 28.6; cholangitis (34% vs. 35%)	44.1 vs. 34.3	253 vs. 262 days	209 vs. 221 days
Ishigaki *et al* [73], 2020	Retrospective	40 vs. 24	100 vs. 96	93 vs. 96	23 vs. 46	10 vs. 12	32.5 vs. 58.3; cholangitis (10% vs. 1%)	48 vs. 43	169 vs. 205 days	238 vs. 381 days

SBS, stent-by-stent; SIS, stent-in-stent; RCT, randomized controlled trial; NA, not available

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Supplementary Table 2 Technical steps to perform an EUS-guided biliary drainage

This approach accesses the bile duct from the stomach to reach the left or right-sided intrahepatic ducts, and thereafter, a communication (permanent fistula) can be created by EUS-HGS or EUS-HDS, respectively.

The steps of an intrahepatic approach to EUS-BD are as follows:

1. A 19-G FNA needle is used to access the left intrahepatic bile ducts in segment 3 from the wall of proximal gastric body or in the duodenal bulb for puncture in the right intrahepatic ductal system
2. Once the needle has been advanced into the duct, bile is aspirated to confirm the position.
3. Then, contrast is injected into the biliary tree to obtain a cholangiogram to confirm the level of obstruction
4. Subsequently, the guidewire is passed (0.025/0.035-inch hydrophilic wire is preferred) to gain access, and is advanced further across the block
5. Once the wire is secure within the biliary tree (either coiled within the dilated intrahepatic ducts or passed through the obstruction into the duodenum), the needle is withdrawn while maintaining access
6. Dilation of this tract is performed to create a permanent fistula (EUS-HGS, EUS-HDS) by cystotome, balloon catheter, bougie catheter
7. Following dilation, a stent is advanced over the wire to complete the HGS/HDS and hence achieve biliary drainage
8. For the bridging method: After obtaining biliary access from the stomach to the left IHBD using a 19-G FNA and a guidewire, the needle is replaced by a standard catheter and a guidewire is advanced through the hilar stricture into the right IHBD. An uncovered bridging SEMS with a thin delivery system is placed across the hilar stricture, followed by a covered SEMS placement from the left IHBD to the stomach, as seen with conventional EUS-HGS

EUS-BD, endoscopic ultrasound-guided biliary drainage; EUS-HGS, EUS-guided hepaticogastrostomy; EUS-HDS, EUS-guided hepaticoduodenostomy; FNA, fine-needle aspiration; IHBD, intrahepatic biliary radicle; SEMS, self-expandable metal stent

Supplementary Table 3 Comparative studies comparing PDT with stent vs. no-stent group in malignant hilar obstruction

Study [ref.], year	Design of study	Etiology	PDT injected	PDT+stent vs. no stent	PDT sessions needed	Endoscopic procedures	Adverse events	Median survival
Ortner *et al* [94], 2003	RCT	CCA; bismuth II-IV	Photofrin 2 mg/kg IV; 630 nm; 180 J/cm^2	20 vs. 19	Mean 2.4	3.8 vs. 3.7 stent exchanges	35% vs. 37%; cholangitis 15% vs. 27%	493 vs. 98 days
Zoepf *et al* [A], 2005	RCT	BDC; bismuth IV	Photosan-3 2 mg/kg; 633 nm; 200 J/cm^2	16 vs. 16	1-2	NA	25% vs. 4%	21 vs. 7 months
Dumoulin *et al* [B], 2003	Retrospective	CCA, bismuth III, IV	Photofrin 2 mg/kg IV; 630 nm; 200 J/cm^2	24 vs. 20	NA	NA	Cholangitis episodes (2 vs. 0 per patient)	9.9 vs. 5.6 months
Kahaleh *et al* [C], 2008	Retrospective	CCA, bismuth I-IV	Photofrin 2 mg/kg IV; 620 nm; 180 J/cm^2	19 vs. 29	1.6 (1-3)	3 (1-8) vs. 2 (1-13) ERCP procedures	Cholangitis 37% vs. 34.5%	16.2 vs. 7.4 months
Witzigman *et al* [D], 2006	Retrospective	CCA, bismuth I-IV	Porfimer 2 mg/kg	68 vs. 56	2 (1-6)	6 (1-19) vs. 2 (1-15) endoscopic procedures	Cholangitis 56% vs. 57%; phototoxicity 12%	12 vs. 6.4 months
Quyn *et al* [E], 2009	Retrospective	CCA, bismuth II-IV	Photofrin 2 mg/kg; 630 nm; 180 J/cm^2	23 vs. 17	1 mean	NA	PDT group: early 30.4%; 17.4%; phototoxicity 17.4%	425 vs. 169 days
Cheon *et al* [F], 2012	Retrospective	CCA, bismuth II-IV	Photofrin 2 mg/kg; 633 nm; 180-200 J/cm^2	72 vs. 71	1 (1-4)	NA	In PDT group: skin pigmentation 14%; bile leak 1 case; sepsis 1 case In Stent only group: cholangitis 16%; 2 cases biloma	9.8 vs. 7.3 months

RCT, randomized controlled trial; PDT, photodynamic therapy; CCA, cholangiocarcinoma; NA, not available

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Supplementary Table 4 Studies on the use of RFA in patients with malignant hilar obstruction

Study (year)	Case number	RFA sessions	Technical success (%)	Clinical success (%)	Adverse events (%)	RBO (%)	Median stent patency	Overall survival
Schmidt *et al* [95], 2016	14	31	100%	-	Overall (28.5%) (cholangitis 2; liver abscess 1; sepsis 1)	Premature stent replacements (<3 mon): 36%	-	-
Inoue *et al* [A], 2020	41	39	39/41 (95.1%)	95.1%	Early 2.4%; later 7.7%	38.5%	230 days	244 days
Bokemeyer *et al* [B], 2019	32 (66% hilar CCA)	54	100%	-	18.5% (cholangitis 11.1%)	-	-	342 days [vs. 221 days (only stent group)]
Tal *et al* [C], 2014	12	19 (1-5)	100%	-	Cholangitis 4 (33.3%); bleeding 3 (25%)	-	-	6.4 months
Kang *et al* [D] 2022	15 (RFA) vs. 15 (stent only)	-	100% vs. 93.3%	100% vs. 86.7%	Early (cholangitis 20% vs. 33.3%); late (cholangitis 33.3% vs. 33.3%; liver abscess 0% vs. 13.3%)	SEMS exchange without PS occlusion: 69.2% vs. 23.1% (only stent)	178 vs. 122 days (only stent)	230 vs. 144 days (only stent)
Oh *et al* [E], 2022	28 (RFA+stent) vs. 51 (only stent)	-	100% vs. 100%	-	Early (7.1% vs. 2%); late (14.3% vs. 3.9%)	67.9% vs. 78.4%	140 vs. 192 days	311 vs. 311 (days)
Inoue *et al* [F], 2022	30	-	93.3%	71.4%	Early 6.7%, late 10%	45%	163 days	262 days
Albers *et al* [96], 2022	42 (RFA) vs. 44 (only SEMS)	-	RFA (100%); stent insertion (98.8%)	-	Overall 10.5% vs. 2.3%; cholangitis 2.6% vs. 0%	-	At 3 mon (73.1% vs. 81.8%); at 6 mon (33.3% vs. 52.4%)	At 3 months (75.5% vs. 73.2%); at 6 months (58.1% vs. 50%)
Dutta *et al* [G], 2017	15 (RFA) vs. 16 (only stent)	1 (1-3)	-	-	3 (20%) (RFA group)	-	220 vs. 106.5 days (intervention free survival)	220 vs. 148 days
Han *et al* [H], 2020	16	3 (1-5)	100%	100%	3 (18.8%) (cholangitis 6.3%)	-	91.5 days	131 days
So *et al* [97], 2022	11	-	100%	72.7%	Cholangitis (18.2%)	Stent dysfunction 72.7%	50 days	289 days

RFA, radiofrequency ablation; RBO, recurrent biliary obstruction; CCA, cholangiocarcinoma; PS, plastic stent

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