Palliative Percutaneous Biliary Interventions in Malignant High Bile Duct Obstruction

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Abstract

Keywords

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The optimal palliative intervention for malignant biliary obstruction is internal drainage by placement of a metallic stent. For patients with hilar biliary obstruction or low bile duct obstruction in whom endoscopy is not feasible, a percutaneous transhepatic approach in interventional radiology is preferred. This article reviews the rationale for this approach, periprocedural management, and techniques to optimize stent patency.

Objectives: Upon completion of this article, the reader will be able to evaluate in what settings percutaneous intervention is appropriate in the setting of malignant bile duct obstruction and discuss what procedure options are available. The reader will also be able to describe the relationship of bacterial colonization of the biliary tract and its impact on future development of cholangitis.

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Malignant biliary obstruction is a debilitating condition that can cause anorexia and pruritus and preclude some systemic therapies. Biliary decompression may be performed by endoscopic, percutaneous, and surgical approaches. Minimally invasive techniques are now standard of care, preferable to surgical bypass^{1,2} because of lower procedure-related morbidity and

shorter overall hospital stay. In the setting of high bile duct obstruction, percutaneous approaches are preferred because a specific segmental duct can be targeted. This is in contradistinction to low bile duct obstruction, in which a single well-placed stent will drain the entire biliary tree and endoscopic interventions are preferred (► **Fig. 1**).³ Furthermore, in some patients with low bile duct obstruction, percutaneous intervention may also be indicated, for example in patients who have undergone pancreaticoduodenectomy for whom endoscopic intervention is particularly challenging or infeasible.⁴

There are several reasons to pursue palliative biliary intervention—to decrease symptoms such as pruritus, to lower the bilirubin level so that the patient can resume palliative systemic therapy, and to treat cholangitis if present.⁵ Percutaneous biliary drains can be painful and problematic for patients, owing to the caustic nature of bile which may inflame the skin near the insertion site, the frequent intercostal positioning of drainage catheters, and the inconveniences of managing a catheter including the inability to bathe and possibility of inadvertent drain retraction.^{6–8} Therefore, the ultimate goal for most biliary procedures for malignant obstruction is to provide completely internal drainage so that the patient does not need to have an external catheter.⁹ This review is therefore focused on the placement and optimization of internal biliary stents in the treatment of malignant high bile duct obstruction.

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Fig. 1 Simple algorithm for management of inoperable biliary obstruction.

Periprocedural Management in Percutaneous Interventions for Biliary Obstruction

Preprocedural workup of candidates for biliary intervention involves laboratory analysis including comprehensive chemistry panel with liver enzymes, complete blood count, and international normalized ratio (INR); contrast-enhanced abdominal CT or MRI of the abdomen; a careful history documenting any prior endoscopic, percutaneous, or surgical intervention; and a medication history including anticoagulant or antiplatelet therapy.⁵ Suggested laboratory criteria for transhepatic biliary procedures include INR < 1.5 and platelet count > 50,000 per microliter; antiplatelet agents should be held for 5 days and fractionated heparin held for 24 hours before the procedure.¹⁰ Key elements to evaluate on imaging include the suspected levels of obstruction, patency of the portal vein, and associated liver atrophy or hypertrophy. These features are critical in choosing an approach to maximize drainage, and to select which patients may be candidates for primary biliary stenting. In addition to patient evaluation, an explicit discussion with the patient and associated care partners is essential in setting expectations, and warning of the possibility that an external catheter may be necessary and/or permanent.⁵

Any intervention in which the biliary tract is entered is at minimum a clean-contaminated procedure (if no signs of infection or contamination are present).¹⁰ Therefore, administration of periprocedural antibiotics is indicated, optimally with an agent with good biliary secretion, such as piperacillin/tazobactam.¹¹ According to Society of Interventional Radiology practice guidelines, routine preprocedure antibiotic prophylaxis is indicated, but there is no consensus on the regimen.¹² Typical bacteria include *Enterococcus* species, gram-negative aerobic bacilli, and *Streptococcus viridans*; consultation with one's institutional infectious disease team is useful in designing routine regimens.

Given that transhepatic biliary interventions have a fairly high rate of infection and bleeding complications, most patients are managed postprocedurally with overnight admission for

observation and treatment of any adverse events that may occur. Beyond infection (cholangitis), potential complications include hemobilia, pericatheter leakage, and pain.^{3,13} In the context of hemobilia, an arterial etiology may be suspected if pericatheter bleeding is observed, or if the bleeding develops weeks after biliary drainage. If an arterial injury is suspected, this should be managed with arteriography and embolization.¹⁴ Insertion site pain is common, particularly for intercostal approaches; intercostal nerve block may be considered if the pain does not improve with time.¹⁵

Serum bilirubin does not immediately decrease following drainage, and may require several weeks to reach the new nadir.⁷ Less than a third of patients who undergo percutaneous biliary drainage to lower the bilirubin for chemotherapy attain a bilirubin level below 1 mg/dL,¹⁶ though nearly 60% attain a bilirubin level below 2 mg/dL.⁷ Depending on which chemotherapy regimen is being considered, serum bilirubin of less than 2 to 5 mg/dL may be sufficient.¹⁷

Hilar Biliary Obstruction and the Papilla

For distal common bile duct stricture, endoscopic therapy is preferred to percutaneous drainage, because endoscopy precludes the possibility of an external biliary drain and there is a reduced risk of hemorrhagic complication.¹⁸ The same is not true, however, for hilar obstructions, where portions of the biliary tract may be isolated from each other. In this setting, percutaneous intervention is preferred because of the ability to target a specific duct/segment.¹⁹

Another potential benefit of a percutaneous approach is maintaining sterility of the biliary tract. Under physiologic conditions when the papilla is intact, the biliary tract is sterile.²⁰ Once the papilla is compromised with an endoscopic procedure (or surgery or fistula), enteric flora colonize the biliary tract that can lead to cholangitis in the setting of future biliary obstruction. Disruption of the papilla has been identified as the major risk factor for future cholangitis after endoscopic intervention.²¹ In patients undergoing percutaneous biliary drainage, prior endoscopic instrumentation and bilioenteric anastomosis are significant predictors of a positive bile culture.²²

When patients who have been previously instrumented present with cholangitis, it is important to identify which sector(s) have been previously contaminated. This way, drainage of the colonized sector(s) can be planned. In the setting of multiple isolated contaminated ducts, effective treatment can require multiple catheters.

Retrospective studies comparing the safety and efficacy of percutaneous versus endoscopic treatment of hilar biliary obstruction demonstrate that percutaneous intervention is associated with reduced time to therapeutic lowering of bilirubin, fewer infectious complications, and repeat drainage procedures.^{8,23–25} For patients with hilar tumors who undergo endoscopic intervention, placement of a unilateral stent, particularly when the bile ducts of both hemi-livers have been opacified with contrast, is associated with significantly worse survival compared with patients who receive bilateral stents.²⁶ The greater the extent of isolation due to the hilar

Fig. 2 Bismuth classification of hilar cholangiocarcinoma. Bismuth 1 is obstruction of the common hepatic duct (proximal to the cystic duct insertion) without extension to the confluence of the right and left hepatic ducts. Bismuth 2 extends to the confluence of the right and left hepatic ducts. In Bismuth 3A and 3B tumor extends to the confluence of the right (3A) or left (3B) sectoral ducts. Bismuth 4 describes tumor extending to both the right and left sectoral ducts, or multifocal tumor.

tumor, the more likely post-endoscopy cholangitis, with Bismuth 1 patients carrying only a 4% risk and Bismuth 3 and 4 patients carrying nearly 60% risk (**► Fig. 2**).²⁷

Given that bacterial colonization occurs with loss of the integrity of the papilla, when percutaneous drainage is performed for hilar obstruction, optimal drain placement may entail a suprapapillary position of the end of the pigtail drainage catheter so as not to introduce enteric flora into the biliary tree. Another potential benefit of suprapapillary catheters (or stents) is a decreased risk of procedure-related pancreatitis.²⁸ As long as there are side holes above and below the obstruction (**► Fig. 3**), these catheters can function as internal/external drains. In a patient with isolated segments, an internal-external drain that terminates in the bowel can result in bacterial colonization of suboptimally drained bile ducts, much like an endoscopic intervention.²²

Fig. 3 Suprapapillary functional internal/external biliary drainage catheter. (a) 3D MRCP image in a patient with metastatic gastric cancer shows a short segment occlusion of the common hepatic duct (arrow) and a normal appearance of the papilla (arrowhead). (b) This finding was confirmed with a cholangiogram performed at the time of biliary drainage (arrow). (c, d) A multi-sidehole drainage catheter (Multipurpose Small Pigtail Drainage Catheter; Cook, Bloomington, IN) was placed with side holes positioned above and below the obstruction. The pigtail (arrow) is above the normal-appearing papilla (arrowhead). This functions as an internal/external drain but maintains the integrity of the papilla and prevents reflux of enteric bacteria into the biliary tree.

Primary Biliary Stenting

In patients who present with elevated bilirubin without cholangitis, percutaneous primary biliary stenting is an excellent option, with the goal for internal drainage without an external catheter. In this setting, primary percutaneous stent placement is associated with nearly 100% catheter-free survival; if a covering catheter is left in place at the end of the case, the majority of patients can have this catheter removed within 24 hours of stent placement.²⁹

The choice of which portion of the liver to drain is based on the nature of biliary isolation and the health/viability of the hepatic parenchyma. The combination of portal vein occlusion and biliary obstruction is associated with atrophy of the involved hepatic segments and compensatory hypertrophy of other liver segments.³⁰ Therefore, efficacy of biliary intervention is optimized when the selected bile duct drains a segment of liver with a patent portal vein; and conversely biliary drainage of atrophic segments should not be expected

to improve function.³¹ At our institution, at the first procedure one bare self-expanding metallic stent (SEMS) is typically placed; if after placement there is good flow through the stent and into the bowel, no covering catheter is left and the tract is embolized with Gelfoam pledgets placed through a sheath (→Fig. 4). Most patients are admitted for overnight observation to monitor for pain requiring intravenous analgesia (5.6%) or fever/leukocytosis requiring intravenous antibiotics (8.5%).²⁹ This procedure is safely performed even in patients with ascites.³²

Median primary patency for single SEMS placed for high bile duct obstruction is approximately 9 months, and for multiple stents it is 7 months.³³ In most cases, partial liver drainage achieves similar efficacy in reducing bilirubin levels compared with multiple stents placed to drain the entire liver.^{34,35} Therefore, single stent placement can be attempted initially and if needed, additional drainage or stent placement can be performed at a subsequent procedure. When stenting of additional sectors is required after the first stent

Fig. 4 Primary biliary stent placement. (a) Contrast-enhanced CT of a 62-year-old woman who had elevated serum bilirubin (6.0 mg/dL), jaundice, and pruritus due to a hilar cholangiocarcinoma (arrowhead) with isolation of the right (arrow) and left hepatic ducts (asterisk). The left hemiliver is atrophic due to obliteration of the left portal vein (not shown). (b) Percutaneous cholangiography demonstrates that the anterior (arrow) and posterior (arrowhead) divisions are not isolated, but the left biliary tract, not opacified (asterisk), is isolated from the right. (c) An 8 mm × 4 cm Wallstent (Boston Scientific, Natick, MA) was placed and balloon dilated (arrow) to 6 mm. (d) After demonstrating good flow through the stent into the duodenum, multiple Gelfoam pledgets (arrow) were placed through the access sheath and the sheath was removed. Jaundice and pruritus resolved within 4 days.

Fig. 5 Placement of a stent through the interstices of an indwelling stent. (a) Coronal contrast-enhanced CT of the liver in a patient with a stent extending to the confluence of the right and left hepatic ducts which are isolated from each other by tumor overgrowth (arrows). The right sided ducts are decompressed, but there is dilation of the left-sided ducts. (b) Images from ERCP performed 5 months later when the patient presented with cholangitis. At ERCP, only a right-sided stent could be placed. The left hepatic duct obstruction was too tight to pass a second stent. (c) Percutaneous cholangiography shows obstruction of the left hepatic duct (arrowhead). Now there are two coaxial stents—the common hepatic duct stent (arrow) and the right hepatic duct stent placed at ERCP (dashed arrow). (d) Primary placement of a left hepatic duct stent through the interstices of the right hepatic duct stent (arrow). (e) Contrast-enhanced CT performed 6 weeks later shows decompressed gas-containing right and left bile ducts.

has been placed, the second stent can be placed next to or through the interstices of the indwelling stent (→Fig. 5). Sometimes, it can be difficult to pass the stent delivery catheter through the interstices of the initial stent, and this can be facilitated by predilation with either a dilator or balloon.

Factors predicting patency of biliary SEMS include duodenal invasion/dysfunction, initial higher bilirubin level, severity of stricture, and perhaps older age.^{36–38} Because patients with duodenal stents often have impaired peristalsis (and hence impaired outflow), in our practice, we generally do not place biliary stents in these patients until they

have passed a capping trial of an internal/external biliary drain. On occasion, we do place primary biliary stents in the setting of a duodenal stent and leave an external drain in place that can be removed in clinic (or bedside) after a few weeks once the patient tolerates a capping trial.

Techniques to Improve Patency of Percutaneously Inserted Biliary Stents

Techniques Using Bare Metallic Stents

Stent size and position, can impact stent patency. For example, 10-mm uncovered metallic stents have significantly better

median patency (186 days) compared with 6-mm uncovered metallic stents (143 days).³⁹ Though not directly compared with prospective studies, in our experience, 8-mm stents perform similarly to 10-mm stents and are preferred when kissing stents are placed.

Many SEMS are approved for use in the biliary tree, and some approved for vascular use are used in the biliary tree off-label. The two major categories include stainless steel stents (e.g., Wallstent; Boston Scientific, Natick, MA) and nitinol stents (e.g., E-Luminexx (Bard Peripheral Vascular, Tempe, AZ), SMART stents (Cordis, Milpitas, CA), Zilver (Cook, Bloomington, IN)). There are several properties to consider when choosing a bare-metal stent including radial strength, foreshortening, and cell design.

The Wallstent is a closed cell design composed of braided stainless steel approved for use in the biliary tract (it is also approved for use in the iliac arteries, tracheo-bronchial tree, venous stenosis, and transjugular intrahepatic portosystemic shunt creation). The stent foreshortens up to 30% from its constrained length after deployment. As the stent is deployed, most shortening is seen at the trailing end, with some additional shortening in the days after deployment as the stent achieves its nominal diameter. Stainless steel stents are typically more radiopaque than nitinol stents; therefore, nitinol stents have radiopaque markers at either ends to enhance visualization. Wallstents can also be reconstrained (recaptured) after deployment of around 60% of the length of the stent. In addition to leading and trailing markers on the delivery device, there is a third marker between the two that indicates the "point of no return." After the stent has been deployed past this marker, it cannot be recaptured. Nitinol stents shorten only around 5%. There are no prospective studies comparing outcomes between stainless steel and nitinol stents in the biliary tree.

Whichever stent is chosen is deployed centered over the obstruction, and choosing an appropriate stent length involves first documenting the length of the obstruction with careful contrast cholangiography. The aim is to cover at least 1 to 2 cm beyond the proximal and distal ends of the obstruction, to prevent tumor overgrowth that can occlude the stent.⁴⁰ This "over-stenting" is particularly important in cholangiocarcinoma because of the tendency of the tumor to grow along the duct.

Uncovered, Covered, and Drug-Eluting Biliary Stents

In the endoscopy literature, it has been shown that uncovered metallic stents outperform plastic stents. Uncovered metallic stent patency, however, may be limited by tumor ingrowth between the interstices of the stent, tumor overgrowth at the margins of the stent, clogging of the stent with food or debris, and epithelial hyperplasia.⁴¹ To address the issue of tumor ingrowth, use of covered self-expanding stents has been proposed as a technique that could prolong patency and delay the need for reintervention.⁴² One caveat is that covered stents are most appropriate for low bile duct obstruction, because use of a covered stent in high bile duct obstruction can jail off ductal branches.

Adoption of covered stents for low bile duct obstruction has been limited by their increased cost, high rates of stent migration, and of the increased incidence of cholecystitis and pancreatitis due to mechanical obstruction of the cystic and pancreatic ducts.⁴³ There are conflicting data regarding whether covered stents impact patency, survival, or cost.⁴⁴ One prospective randomized trial compared endoscopically placed covered and uncovered stents in 112 patients with unresectable distal malignant biliary obstruction. Stent occlusion occurred in 14% of the patients in the covered SEMS at a mean of 304 days compared with 38% occlusion in the bare metal SEMS at 166 days. Two patients in the covered SEMS group had acute cholecystitis (vs. none in the bare metal cohort) and five patients in the covered SEMS group had mild pancreatitis compared with one in the bare metal.⁴⁵ More recently, a prospective randomized trial of 400 patients who underwent endoscopic stent placement with either bare metal or covered stents found no difference in stent patency, survival, or complication rates, although they did observe significantly more stent migration in the covered stent cohort.⁴⁶

While case series describing the feasibility of covered stent placement via percutaneous approaches have been published,⁴⁷ prospective comparative trials are lacking. There is therefore insufficient evidence to recommend the use of covered biliary stents during percutaneous primary biliary stenting.

Another technique proposed to combat both tumor ingrowth and epithelial hyperplasia (and biofilm) is use of drug-eluting stents. A small series described the feasibility of endoscopically placed paclitaxel-coated metallic stents in malignant biliary obstruction.⁴⁸ This was a single-arm study of 21 patients with low bile duct obstruction treated with 10 mm stents. Mean stent patency was 429 days (14.1 months) and mean survival was 350 days. Out of 21 patients, 9 experienced stent occlusion due to clogging in 4 patients; tumor overgrowth in 3 patients, and tumor ingrowth in 2 patients. This was followed by a prospective study of 106 patients with low bile duct obstruction treated with drug-eluting or covered SEMS. The authors found no difference in patency or survival rates, though the studies may have been underpowered.^{49,50} At this time, there is no helpful evidence describing the use of drug-eluting stents in percutaneously placed biliary stents, and no drug-eluting stents are Food and Drug Administration (FDA) approved for biliary indication.

Percutaneous Intraductal Procedures

Radiofrequency ablation (RFA) delivers high-frequency alternating current to generate friction and cause coagulative necrosis. The Habib Endo HPB (EMcision) is a single-use FDA-approved over-the-wire 8-Fr bipolar RFA catheter that can be used at the time of SEMS placement or to restore patency of stents occluded by tumor ingrowth. At the distal end of the catheter are two 8-mm stainless steel electrodes separated by 6 mm for a total coverage of 21 mm which creates an ablation zone of up to 25 mm in length and 9 mm in diameter. The typical ablation is performed at 10 to 20 W for 90 to 120 seconds. The RFA catheter can be advanced over a wire and positioned within the occluded stent. After RFA debris is swept through with an occlusion balloon,

cholangiography is performed to ensure patency. More recently, the Habib percutaneous HPB catheter has been used to perform RFA from a percutaneous approach. This technique was shown to be feasible and safe in a series of 39 patients with both high and low malignant bile duct obstruction.⁵¹ The same device was used successfully in nine patients with obstructed SEMS to reestablish stent patency without the need for additional stent placement.⁵²

Intraductal brachytherapy is similar to intraductal ablation in that it can prevent tumor ingrowth. Brachytherapy, similar to RFA, can deliver a high dose to target tissue within approximately a 1-cm diameter while sparing surrounding tissues because the dose drops quickly with distance. Brachytherapy can be performed during SEMS placement or biliary drainage. A blind-ended graduated brachytherapy catheter is placed 1.5 to 2 cm past the distal end of the stricture. The target is determined by the graduations on the catheter and the catheter is affixed to the patient. The patient must be transferred to a radiation suite (iridium-192) to deliver up to 800 cGy radiation. The brachycatheter can then be removed if a stent is in place, or exchanged for a biliary drain if a second dose of radiotherapy is planned. In a pilot study of 18 patients, the feasibility and safety of intraluminal brachytherapy in two fractions separated by 1 week was established. However, because all patients had internal external drains, the effect on stent patency could not be determined.⁵³

An interesting combination of biliary drainage and brachytherapy involves the placement of a strand of iodine-125 seeds placed in and affixed to the biliary drainage catheter.⁵⁴ One benefit of this technique is that it may be performed entirely in the interventional suite. This small study demonstrated prolongation of stent patency by 3 months. A subsequent randomized study of 23 patients comparing conventional biliary stents to stents loaded with iodine-125 seeds showed statistically significant prolongation of stent patency by nearly 5 months, although the median conventional stent patency of 2.5 months was shorter than usual.⁵⁵

Compared with the relatively disappointing results with covered stents, early studies suggest that intraductal ablation and radiation are promising. Ideally, these preliminary results will be followed by larger prospective comparative studies to establish the superiority of these approaches during primary biliary stenting and reinterventions.

Conclusion

Inoperable malignant biliary obstruction causes significant impairment in quality of life and can interfere with the administration of palliative chemotherapy. Hilar obstructions are best managed with percutaneous approaches to allow for targeting of a specific duct and avoid the possibility of contaminating the biliary tract by violating the papilla. To optimize patient comfort, the goal in many cases can be primary SEMS terminating above the papilla. This technique is safe and effective in many patients. Emerging techniques such as intraductal ablation or brachytherapy may prolong stent patency and minimize the need for reintervention.

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