

# Percutaneous Management of Malignant Biliary Strictures: Current Status and Future Directions

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## Abstract

### Keywords

- ▶ malignant biliary obstruction
- ▶ percutaneous interventions
- ▶ biliary drainage
- ▶ biliary stents

Various minimally invasive percutaneous interventions may be performed for the treatment and management of malignant biliary obstruction. The types of percutaneous interventions include percutaneous transhepatic biliary drainage, percutaneous cholecystostomy, and biliary stent placement. Biliary stents have undergone continued evolution in design to prolong patency, increase cost-effectiveness, improve patient survival, and quality of life. Furthermore, investigational techniques such as radio-frequency ablation, intraluminal brachytherapy, and photodynamic therapy promise new technologies in the field of biliary intervention. This review focuses on the current status of percutaneous therapies for malignant biliary strictures and obstruction.

Biliary obstruction manifests as abnormal luminal narrowing of the biliary tree, which impedes the normal physiologic flow of bile to the small bowel. The etiology of biliary obstruction is often divided into benign and malignant causes, which may be difficult to distinguish at presentation but is nonetheless imperative to guide management and determine prognosis. Patients with benign biliary obstruction often have a good prognosis and do well after intervention while those with malignant biliary obstruction (MBO) often present at a later stage and have a poor prognosis.

Although the clinical incidence of neoplasms that cause MBO is relatively low, there has been increasing incidence by estimates from the Surveillance, Epidemiology, and End Results database from North America.<sup>1</sup> Malignant biliary obstructions are caused by either external compression or infiltration of the biliary tree by the tumor. The most common malignancies that cause MBO are cholangiocarcinoma and adenocarcinoma of the pancreas, but gallbladder, gastric, and ampullary/duodenal malignancies in addition to lymphoma, intrahepatic metastasis, and metastatic lymphadenopathy may also be causative.

Clinical presentation of MBO is dependent upon the etiology. Patients with intrahepatic cholangiocarcinoma often present with abdominal pain, night sweats, and cachexia.

Those with extrahepatic or distal tumors often present with obstructive symptoms of jaundice or pruritus. In fact, obstructive jaundice is the most common clinical presentation and chief presenting symptom in 70% of patients with pancreatic cancer at the time of diagnosis.<sup>2</sup> Untreated MBO may also cause cholangitis or sepsis due to increased bowel wall permeability, portal system bacteremia, and impaired liver T-lymphocyte function.<sup>3,4</sup>

The management of patients with MBO usually requires a multidisciplinary approach within tertiary care centers. Clinical expertise from oncologists, hepatologists/gastroenterologist, hepatobiliary surgeons, radiologists, interventional radiologists, and radiation oncologists is necessary for successful treatment. Interventional radiologists may be asked to provide percutaneous biliary decompression for palliation or preoperative drainage in those with resectable disease.<sup>5–7</sup> Klatskin's initial observation that patients with cholangiocarcinoma die from biliary obstruction rather than metastatic disease still holds true and local tumor control is important for patient survival.<sup>8</sup> Though biliary decompression may not improve survival, palliative therapy reduces the risk of sepsis, improves the liver function that is a prerequisite for initiation of chemotherapy, resolves jaundice, and decreases pain.

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Herein, we review the role of interventional radiology in the treatment and management of patients with malignant biliary obstruction.

## Role of Diagnostic Radiology

Ultrasound (US) is an invaluable diagnostic modality for the initial assessment of patients with suspected hepatobiliary pathology. Real-time US imaging allows assessment of the hepatic parenchyma and biliary tree, presence of ascites, and biliary confluence patency. Evaluation of the distal common bile duct, however, is often limited such that additional evaluation usually requires cross-sectional imaging with computed tomography (CT), magnetic resonance imaging (MRI), and/or magnetic resonance cholangiopancreatography. These imaging modalities help determine the cause of biliary obstruction and define the extent of disease, level of obstruction, and biliary anatomy. Ultrasound and CT may also be used for histopathologic confirmation by either interventional radiology (US- or CT-guided biopsy) or endoscopically using endoscopic retrograde pancreatography (ERCP) or endoscopic US-guided fine needle aspiration. Positron emission tomography/CT has a role in detecting distant and nodal metastasis although its use in the diagnosis of cholangiocarcinoma is not well established.

## Percutaneous Techniques

There have been multiple advances in radiology and percutaneous intervention since Burckhardt and Muller performed the first radiologic visualization of the biliary tree by puncture of the gallbladder in 1921.<sup>9</sup> The first percutaneous transhepatic cholangiography (PTC) was performed by Huard et al<sup>10</sup> 16 years later. Despite the use of multiple methodologies and techniques, it was not until the use of the fine needle technique developed at Chiba University and presented by Oto et al that resulted in a significantly decreased complication rate.<sup>11</sup> These advances ultimately shifted palliative therapy from surgery to percutaneous or endoscopically placed stents. Similarly, stents have undergone a significant evolution in design from plastic to bare metallic to covered metallic and ultimately to drug-eluting stents. Stent evolution is driven by the desire to maintain stent patency, decrease tumor ingrowth, and increase procedure cost effectiveness.<sup>12,13</sup> Moreover, aside from percutaneous stent placement, minimally invasive palliative therapy has also been performed with intraluminal brachytherapy, endoluminal biliary radiofrequency ablation (RFA), and photodynamic therapy (PDT).

## Percutaneous Transhepatic Biliary Drainage

For patients who will undergo surgical excision of an obstructing mass, preoperative biliary decompression may provide normalization of liver enzymes and bilirubin levels while limiting the risk of ascending cholangitis. Access for percutaneous transhepatic biliary drainage (PTBD) may be from the right or left liver lobes depending upon the extent of

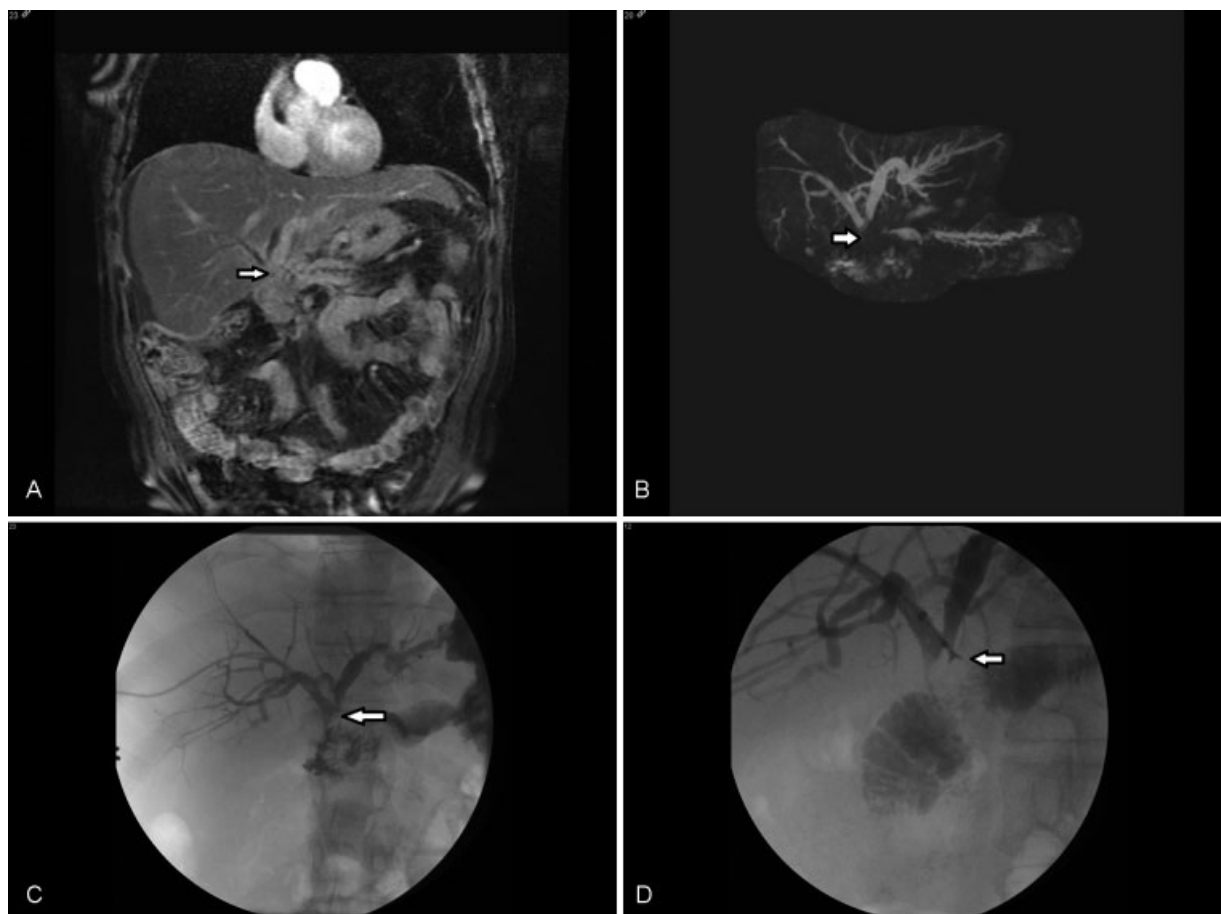
biliary obstruction. Once access to the biliary system is obtained with a needle (e.g., Chiba), a cholangiogram defines the biliary anatomy and characterizes the obstruction. A hydrophilic guide wire is placed across the stricture, the tract is dilated, and an internal–external drainage catheter is positioned across the stricture (i.e., the tip of the catheter in the bowel). If initial attempts to cross a stricture fail, an external-only drain may be left in place to reduce inflammation and decompress the biliary so that reattempt at internalization may be successful. A PTBD may be technically limited secondary to nondistention of the biliary system, but interestingly there is no difference in success rates between dilated and nondilated biliary systems.<sup>14,15</sup>

## Percutaneous Cholecystostomy

Percutaneous cholecystostomy is usually performed for decompressing an inflamed gallbladder in a patient who cannot undergo surgery at the time of presentation. Percutaneous cholecystostomy may also be performed as an alternative to PTBD when the biliary ducts are not adequately dilated. This may be performed via a transhepatic or transperitoneal approach. In the transhepatic approach, the drainage catheter traverses a portion of the liver before entering the gallbladder; this provides catheter support and decreased risk of an intraperitoneal biliary leak. In the transperitoneal approach, the gallbladder is punctured directly. Trocar or Seldinger approaches may be utilized for both techniques. Catheters are usually kept in place for 2 to 3 weeks to allow for tract maturation. Access through the gallbladder may be used to treat MBO via stent placement.<sup>16,17</sup> Complications may include catheter dislodgement, pain, bleeding, pneumothorax, fistula formation, or biliary peritonitis.

## Biopsy

If the diagnosis or etiology of an MBO remains unclear with cross-sectional imaging, tissue collection utilizing brush cytology or forceps biopsy can provide a definitive diagnosis. Brush cytology is typically performed during ERCP and is considered safer and technically easier than a forceps biopsy. Several studies have attempted to quantify the sensitivity of each technique. One study in which brush cytology was performed during percutaneous biliary drainage demonstrated sensitivity, specificity, positive predictive value, negative predictive value, and accuracy of 75, 100, 100, 12.5, and 75.9%, respectively.<sup>18</sup> The sensitivity of brush biopsy in the diagnosis of cholangiocarcinoma was greater than in those with non-cholangiocarcinoma.<sup>18</sup> Forceps biopsy is unique in that unlike brush cytology, it provides a sample of the subepithelial stroma (–Fig. 1). In a published series of 130 patients with MBO who underwent forceps biopsy after PTBD, the sensitivity, specificity, and accuracy were 78.4, 100, and 79.2%, respectively.<sup>19</sup> In another published series, forceps biopsy was found to have a sensitivity of 71%.<sup>20</sup> A study comparing brush cytology with clamshell forceps under choledochoscopic guidance and clamshell forceps found that utilization of clamshell forceps with cholangioscopy was more sensitive than the other



**Fig. 1** A 74-year-old woman presents with recurrent cholangitis. (A) Coronal gadolinium-enhanced T1-weighted fat-saturated image demonstrates ill-defined stricture at the level of the hilum (arrow) with intrahepatic ductal dilatation. (B) Coronal T2-weighted MR cholangiopancreatography image demonstrates abrupt cutoff of both right and left intrahepatic ducts (arrow). (C) Percutaneous transhepatic cholangiography demonstrates severe narrowing of the common bile duct (arrow). (D) Biopsies were taken using a forceps device (arrow). MR, magnetic resonance.

two techniques but was not statistically significant.<sup>21</sup> A more recent study comparing brush cytology versus forceps biopsy found sensitivity, specificity, and accuracy for brush cytology versus forceps biopsy were 47.8, 100, 69.2%, and 92.1, 100, 93.6%, respectively.<sup>22</sup> A study comparing forceps biopsy versus a modified cytology sampling in which cytological sampling was obtained by washing the forceps device in cytological solution demonstrated sensitivity for forceps biopsy and forceps wash cytology of 78 and 61%, respectively.<sup>23</sup> Kim et al have found that the addition of bile cytology from forceps biopsy can increase sensitivity and may be a complementary diagnostic tool for diagnosing cholangiocarcinoma. In their retrospective series of both endoscopic and percutaneous intervention which included 766 patients sensitivity for bile cytology, forceps biopsy, and utilization of both was 24.7, 74.4, and 77.9%, respectively.<sup>24</sup>

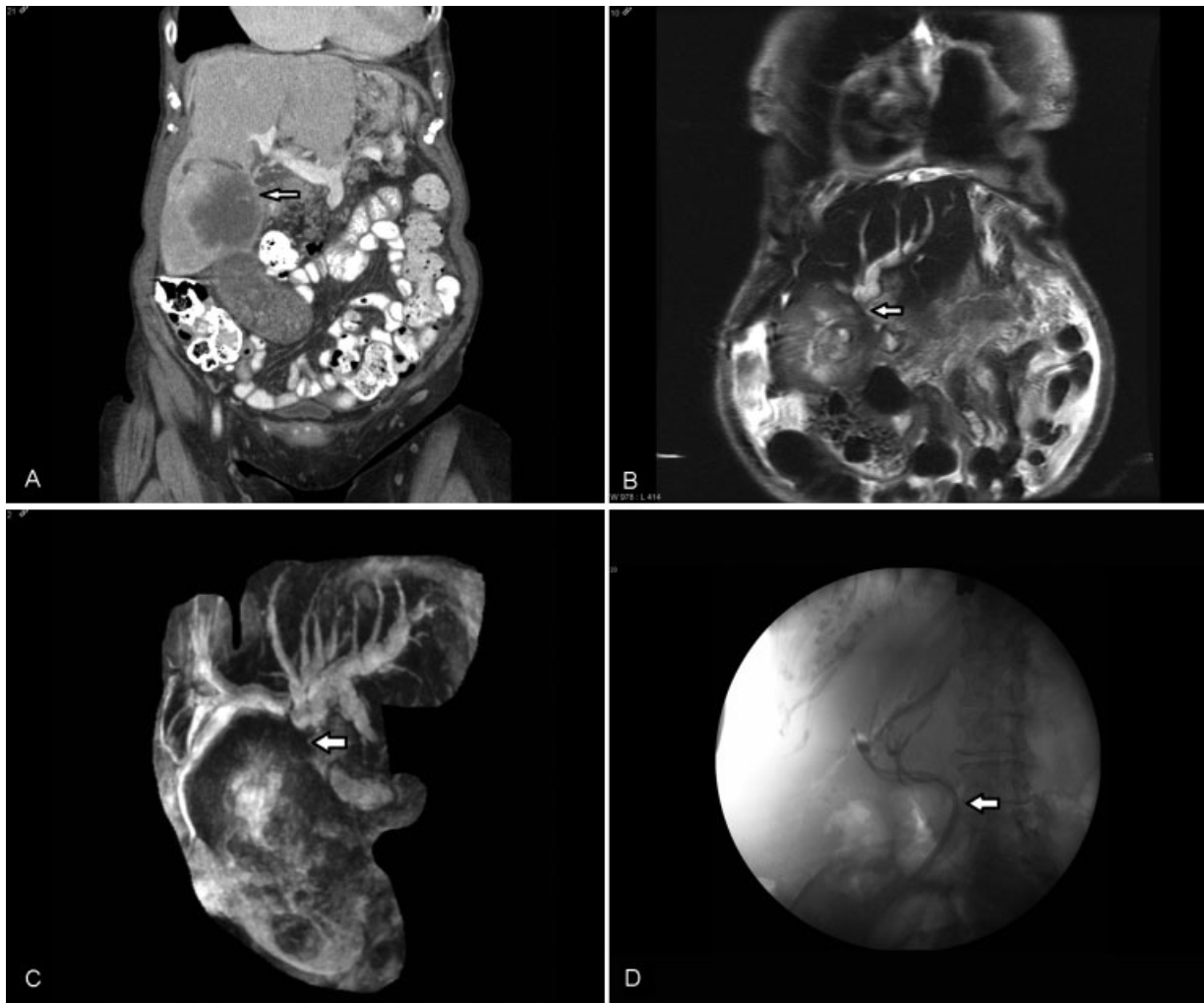
### Portal Vein Embolization

In patients undergoing hepatectomy, portal vein embolization (PVE) may be performed as an adjunct to induce compensatory enlargement of the liver remnant.<sup>25</sup> Hemming et al demonstrated that in those patients in whom liver resection would ultimately result in future liver remnant

volume of less than 25%, PVE was not associated with pre- or postoperative complications. Moreover, patients who did not receive PVE had longer hospital stays and had a higher incidence of hepatic failure. Uhl et al noted that PVE of portal vein segmental branches 4–8 resulted in average volume increase in segments 2 and 3  $280 \pm 95$  mL to  $420 \pm 98$  mL within 6 weeks.<sup>26</sup>

### Plastic versus Metallic Stent

Plastic stents were the first type of stents developed for the treatment of MBO but were problematic due to their small size of 12F (the maximum size that could fit through the endoscope) or 14F when placed percutaneously, and propensity for occlusion. Moreover, the supplemental addition of antibiotics and/or ursodeoxycholic acid has not been shown to increase stent patency.<sup>27</sup> Self-expandable bare metallic stents (SEMS), capable of expansion to 30F, were developed to overcome these problems (–Fig. 2). Multiple studies have demonstrated that SEMS provide significantly longer patency periods than plastic stents.<sup>28–32</sup> Moreover, the superiority of SEMS compared with plastic stents have been further supported by meta-analyses and randomized clinical trials.<sup>33–35</sup>



**Fig. 2** An 82-year-old female patient chronic thrombocytopenia, mechanical mitral valve replacement, atrial fibrillation on warfarin presenting with abdominal pain and elevated liver function tests. (A) Coronal gadolinium-enhanced CT in portal venous phase reveals a large gallbladder adenocarcinoma extending into and involving liver segment 5 with associated common bile duct narrowing and intrahepatic ductal dilatation (arrow). (B) Coronal T2-weighted single shot fast spin echo MR image demonstrates gallbladder mass obstructing the left hepatic bile duct system (arrow). (C) 3D reconstructed MR cholangiopancreatography images revealing common bile duct obstruction due to gallbladder lesion (arrow). (D) Self-expandable metal stents were inserted endoscopically (arrow). 3D, three-dimensional; CT, computed tomography; MR, magnetic resonance.

SEMS are made from either stainless steel (cobalt-chromium) or nitinol (nickel-titanium) mesh that allows the stent to embed into the biliary wall, thereby decreasing the risk of migration. The disadvantage to SEMS, however, is that the mesh-like structure of the stent may result in neoplastic tissue in-growth and ultimately occlusion. The combination of tumor ingrowth, epithelial hyperplasia, bio-film deposition, and sludge limits the median patency to 120 days.<sup>36</sup> Occlusion of SEMS ranges from 20 to 50%.<sup>28,31,37</sup> Another disadvantage of SEMS is that they are not removable or interchangeable and therefore must be utilized in the appropriate clinical scenario. Self-expandable metal stents are, however, much less expensive than covered SEMS.

### Covered Biliary Stents

Covered SEMS (CSEMS) are similar to SEMS in their tubular design but are covered by a thin membrane that theoretically prohibits tumor in-growth (→Fig. 3). Since CSEMS are not

embedded in the biliary wall, they are removable but also prone to migration. Because CSEMS are removable, some advocate their use when the histological diagnosis is unclear while uncovered SEMS should be used for confirmed malignancy. Multiple antimigrational covered stents have also been developed. Isayama et al described a modified Zeo stent with flared ends which effectively, though not completely, prevented stent migration.<sup>38</sup> A randomized trial with 120 patients showed an increased stent patency with antimigration covered stent compared to uncovered stents (187 vs. 132 days).<sup>39</sup>

Published studies demonstrate conflicting evidence as to whether CSEMS increase stent patency. A meta-analysis by Saleem et al found that CSEMS had longer stent patency times significantly as compared with uncovered stents.<sup>40</sup> A more recent meta-analysis, however, showed no difference in patency periods between the two types of stents.<sup>41</sup> Randomized trials have shown no difference in stent patency or patient survival between the two groups.<sup>42,43</sup>



**Fig. 3** A 57-year-old male patient with, history of esophageal cancer, presents with jaundice and abdominal pain. (A) Coronal contrast-enhanced CT in portal venous phase demonstrates intrahepatic duct dilatation at the level of the porta hepatitis (arrow) due to a malignant stricture. (B) Percutaneous transhepatic cholangiography with the placement of a 10 mm × 6 cm covered metal stent (arrow).

The catheter delivery system of the CSEMS is larger than SEMS. A measuring pigtail may be used for accurate deployment of the covered stent to minimize the risk of blocking the cystic duct. The covering membrane can be made of multiple materials including polyurethane, silicone, or expanded-polytetrafluoroethylene/fluorinated ethylene propylene (ePTFE/FEP). Polyurethane covered stents have shown limited efficacy in prolonging stent patency compared with uncovered SEMS.<sup>44–46</sup> ePTFE/FEP covered stents seem to be effective in providing biliary drainage.<sup>47–49</sup> Disruption of the polymer cover can occur either through mechanical damage related to stent microfracture during placement or through a chemical process. Chemical degradation can occur by exposure to bile, acidic gastric contents, and/or pancreatic enzymes.<sup>50</sup> Decreased porosity of ePTFE/FEP grafts has been shown to decrease the incidence of stent occlusion and sludge incrustation.<sup>47–49</sup>

### Drug-Eluting Stents

Drug-eluting stents (DES) may be an alternate treatment modality for MBO in the future. Currently, there are few

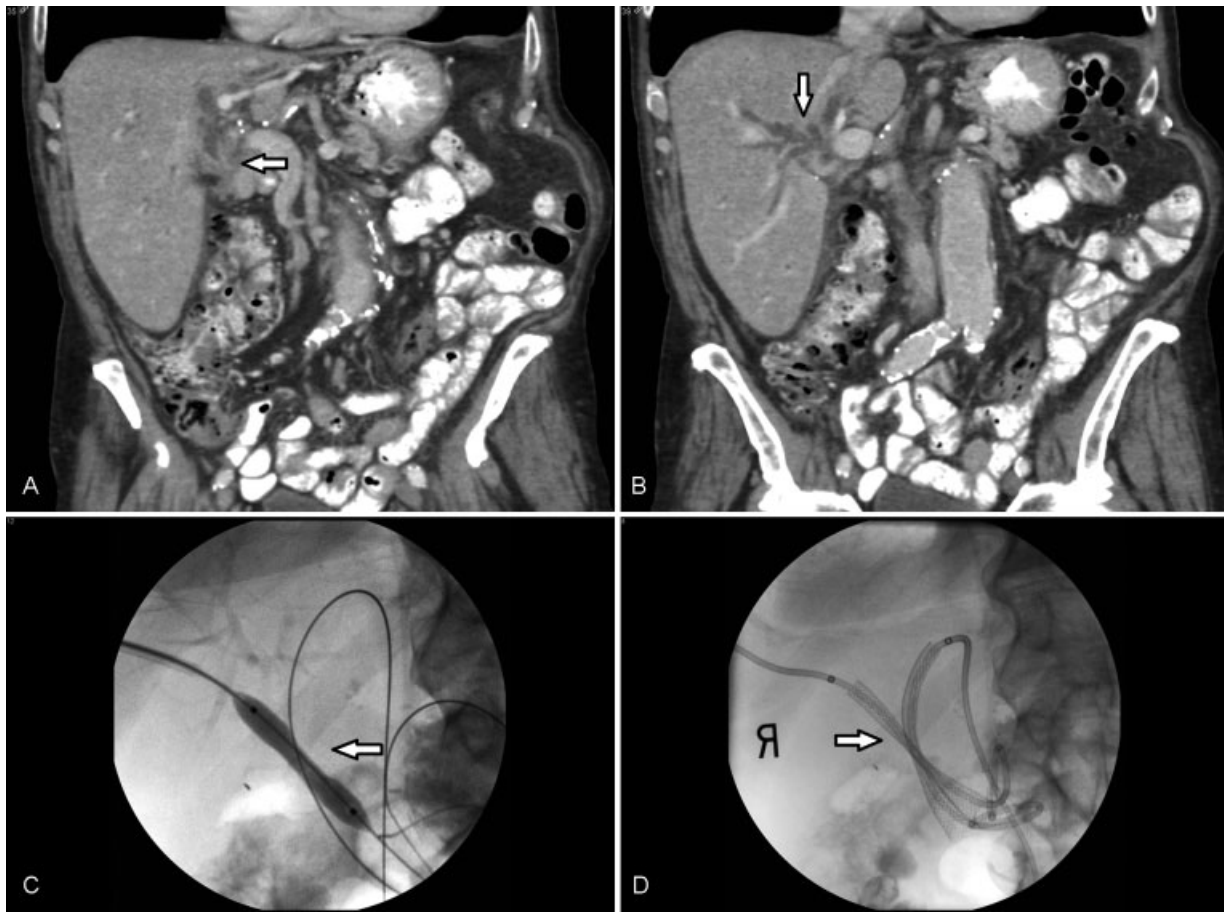
published studies regarding DES. Mezawa et al described the use of a carboplatin biliary drainage tube in five patients with inoperable cholangiocarcinoma and reported the DES was well tolerated and had an efficacy of 60%.<sup>51</sup> Suk et al published the first biliary study of paclitaxel-DES in humans concluding that DES are effective, safe, and technically feasible.<sup>52</sup> Song et al published a prospective randomized trial comparing paclitaxel-DES to control CSEMS in patients with MBO in 49 patients and found that DES provided no advantage regarding stent patency or patient survival compared with the control group.<sup>53</sup> Stent in-growth occurred in 5/24 patients in the DES group compared with 4/25 in the control group. Much research and higher powered studies are necessary to determine the potential advantages of DES over conventional covered stents.

### T, Y, and X (Crisscross) Configured Stents

Malignant hilar obstruction is most commonly caused by cholangiocarcinoma and can be difficult to treat. Cholangiocarcinoma occurs at the confluence of the left and right hepatic ducts in 60 to 70% of the cases, distal common bile duct in 20 to 30% of the cases, and intrahepatic ducts in 5 to 10% of the cases.<sup>54</sup> In 1975, Bismuth and Corlette classified malignant hilar stenosis into four categories based on the extent of involvement of the common hepatic, left, and right bile duct.<sup>55</sup> Type I obstruction involves the common hepatic duct (CHD) with preservation of the confluence. Type II obstruction involves the CHD as well as the confluence of the left and right ducts. Type IIIA obstructions involve the CHD and right hepatic duct at the confluence and type IIIB involve the CHD and left duct. Type IV injuries extend to the bifurcations of the left and right hepatic ducts. Percutaneous or endoscopic intervention is the mainstay of palliative treatment as only 20 to 30% of tumors are resectable.<sup>56</sup>

Controversies exist as to whether partial/unilobar or total/bilobar/bilateral drainage should be performed for palliative therapy. Advocates of partial/unilateral drainage emphasize lower complication rates associated with a minimally invasive approach.<sup>57</sup> Some investigators call for complete drainage<sup>58</sup> while others still advocate for a stepwise approach (i.e., placement of a single stent and assess for clinical response, then place a second stent if necessary).<sup>59</sup> Others advocate for unilobar drainage in Bismuth I–III obstructions and bilobar drainage in type IV obstruction.<sup>60</sup> Regardless, bilateral biliary drainage may be beneficial in some patients to prevent cholangitis, preserve liver function, and has been associated with better survival rates.<sup>61</sup> Multiple stents and techniques have been developed for the bilateral palliative treatment of malignant hilar obstruction.

Currently, two techniques have been developed for percutaneous placement of bilateral SEMS, including the side-by-side (SBS) and stent-in-stent (SIS) deployment techniques (►Fig. 4). SBS technique results in deployments of SEMS in a parallel configuration. This configuration may prevent full expansion or result in the collapse of one or both stents. Interestingly, an endoscopic series comparing the SBS to SIS techniques demonstrated that the complication rates were



**Fig. 4** A 77-year-old male patient presents with jaundice, malaise, fatigue, and a 15 lb weight loss over 2 weeks. (A) Coronal gadolinium-enhanced CT in portal venous phase demonstrates smooth narrowing with some enhancement of the common bile duct at anastomosis (arrow), upstream dilatation of CBD, and intrahepatic biliary duct consistent with anastomotic stenosis due to bile duct adenocarcinoma. (B) Coronal gadolinium-enhanced CT in portal venous phase demonstrates upstream dilatation of CBD and intrahepatic biliary ducts (arrow). (C) Balloon dilatation of the malignant stricture (arrow) with a noncompliant 8 mm balloon. (D) Two crisscrossing (arrow) 10 mm × 6.8 cm covered metal biliary stents were placed via a percutaneous approach. CT, computed tomography.

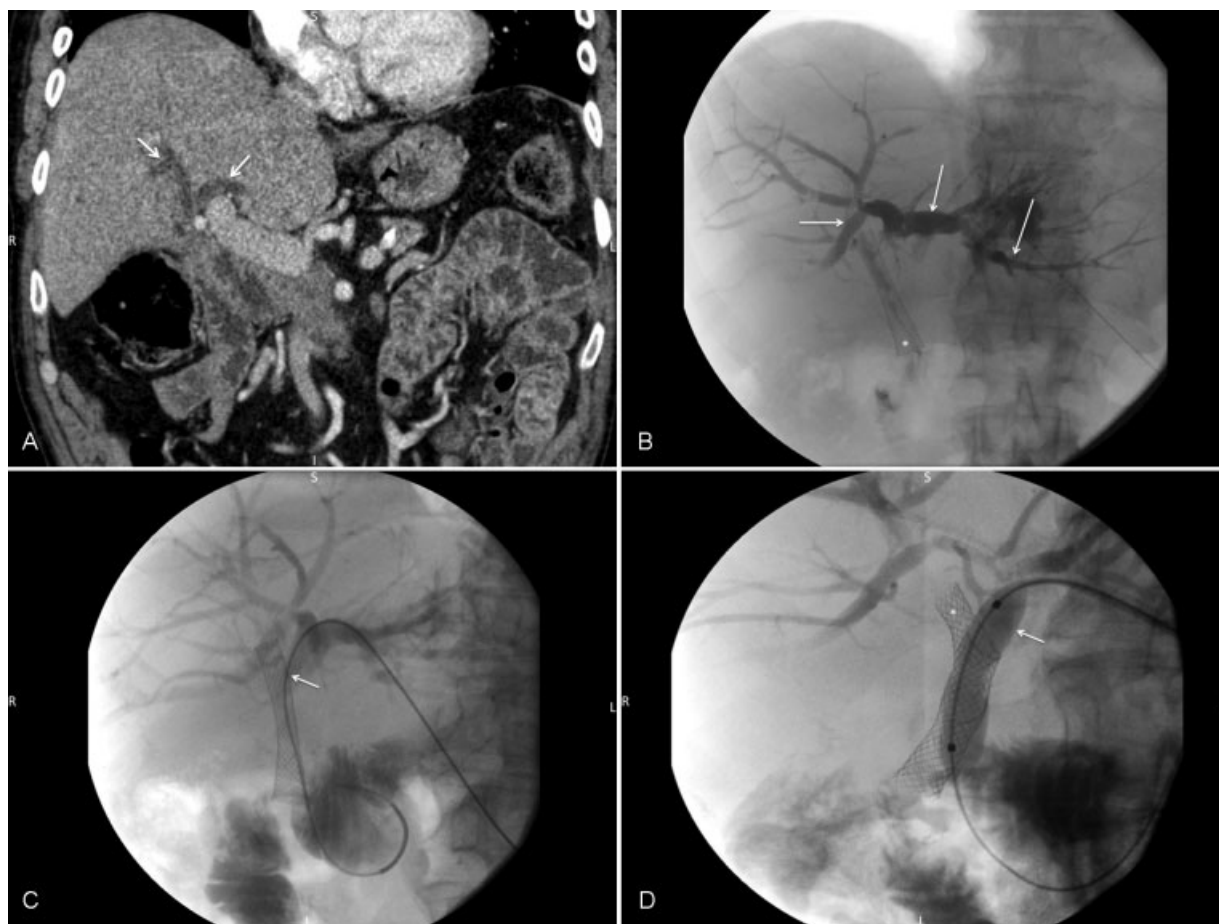
higher in SBS deployment; however, SBS tends to be associated with higher patency rates.<sup>62</sup> In the SIS technique, a stent is deployed through the mesh of the first stent. This may prevent stent displacement.<sup>63</sup> Open cell designs have been developed to overcome the technical difficulties of SIS deployment and allow easier connectivity between stents as opposed to the traditional closed cell designs. Both techniques may be utilized for T-configured or Y-configured stents.

Y-stents are composed of two components, including the main frame and a long contralateral limb stent. The main piece consists of a common bile duct (CBD) section (uncovered), a covered long limb, and a covered short limb. A secondary covered stent is later mated to the short limb creating the full “Y” configuration (→ Fig. 5). In a prospective pilot study including 20 patients, Gwon et al demonstrated that ePTFE covered Y-configured stents (ComVi stent; TaeWoong Medical, Seoul, Korea) are safe and clinically effective in the palliative treatment of hilar biliary obstruction.<sup>64</sup> There were minor complications of self-limiting hemobilia in one patient and rapidly resolving cholangitis in three patients. Similar outcomes have been demonstrated with silicone covered nitinol Y-configured stents (EGIS Biliary KEY stent; S&G Bio, Seoul,

Korea)<sup>65</sup> and self-expandable nitinol stents (8.5F, Niti-S Biliary Y-type, Taewoong Medical).<sup>66</sup> Generally, complication rates during Y-configured stent placement are low with the technical success achieved in most cases.

The transhepatic or T-configured stents have also been used with success. The T-configured stents have a horizontal stent that bridges the right and left hepatic ducts and a vertical component that extends into the common bile duct. T-configured stents have been made with multiple grafts or membranes. No study has demonstrated superiority between Y- and T-configured stents, but some authors believe that T-configured stents may have some advantages. Kim et al argue that T-configuration offers a large luminal diameter throughout the biliary system which can be placed through a single access, is safe, and reliable. Also, overlapping endoprostheses may prevent stent migration.<sup>63</sup>

In certain situations, hilar malignancy may extend beyond segmental ducts causing multiple intrahepatic obstructions in which T- and Y- configured stents may not provide adequate drainage. In such instances, crisscrossing or X-configured stents may be beneficial (→ Fig. 4). This entails crossing stents to drain two right sector ducts and a left



**Fig. 5** (A) Contrast material-enhanced coronal CT scan in a patient who is s/p Whipple procedure for adenocarcinoma of the pancreas. White arrows point to dilated left and right bile ducts. (B) Percutaneous transhepatic cholangiogram that demonstrates a metal stent with the right hepatic duct (white asterisk) and dilates intrahepatic bile ducts (white arrows). (C) Image from percutaneous cholangiogram that demonstrates a guidewire and catheter that was placed into the biliary stent and the bowel. (D) The fluoroscopic image that demonstrates 10 mm balloon (white arrow) distention of metal stent (asterisk). (E) The fluoroscopic image that demonstrates new metal stent (white arrow) in the left biliary tree that has been placed through an existing right-sided biliary stent. (F) Contrast material-enhanced coronal CT scan in a patient who is s/p Whipple procedure for adenocarcinoma of the pancreas and percutaneous biliary stent placement in a Y-configuration. White arrows point to metal stents within the left and right bile ducts. CT, computed tomography.

hepatic duct for trisectoral drainage. Placement of the stent depends on the biliary anatomy. If standard anatomy exists, a stent may be placed in the right anterior duct to the left hepatic duct and another stent from the right posterior duct to the common bile duct. Bae et al have demonstrated that this configuration is feasible, safe, and effective.<sup>67</sup> A downside to X-configured stents is that they may require multiple hepatic access points. At present, X-configured seems to be noninferior to T- and Y-configured stents; however, further investigation is needed to determine if trisectoral drainage provides durability over other methods.

### Intraluminal Brachytherapy

Intraluminal brachytherapy (ILBT) aims to treat malignant obstruction by the insertion of radioactive implants or pellets directly into tissue, minimizing radiation risk to adjacent organs.<sup>68,69</sup> ILBT is most commonly used for the treatment of localized prostate cancer but recently has also been used for inoperable biliary malignancies. Iridium-192 is

a gamma emitter, which has produced promising results for the treatment of inoperable biliary tumors. Published studies have demonstrated that ILBT is safe and technically feasible without major complications and positive impact on the quality of life.<sup>70,71</sup> Moreover, the combination of percutaneous stenting and ILBT has been described. Eschelmann et al reported on a series of 22 patients with unresectable biliary obstruction caused by either cholangiocarcinoma or secondary extrahepatic bile duct malignant tumors who underwent stenting and radiation therapy (average 25 Gy), including ILBT with Ir-192 and found increased stent patency and survival in the cholangiocarcinoma group.<sup>72</sup> Conversely, Takamura et al described a multimodality approach (ILBT, external beam radiation therapy, and biliary stenting) that did not impact survival or biliary patency in 93 patients but improved the quality of life in those with extrahepatic bile duct carcinoma.<sup>73</sup> Similarly, Isayama et al found that external beam radiotherapy improved patient prognosis and patency of SEMS but ILBT provided no additional benefit.<sup>74</sup> Patients with inoperable extrahepatic bile duct malignancy who

underwent EBRT compared with those with EBRT and ILBT had no difference in recurrence rates (53 vs. 36%) but prolongation of the median time to tumor recurrence 5 versus 9 months.<sup>75</sup>

## Radiofrequency Ablation

Radiofrequency ablation (RFA) is a technique in which rapidly alternating electric current causes vibrational movement of ions, resulting in frictional heat that leads to coagulative necrosis. RFA has been described in primary and secondary hepatic cancers<sup>76–78</sup> but its novel use for bile duct cancers has not been described until recently. In vivo and ex vivo animal experiments provided the basis upon which the first human use of radiofrequency treatment was performed by Steel et al in 2011 in 22 patients with pancreatic and cholangiocarcinoma.<sup>79–81</sup> In Steel et al's experimental design, RFA was applied endoscopically before the application of SEMS. It concluded that endobiliary RFA is a safe treatment option; however, its efficacy at providing long-term stent patency remains to be proven in future randomized studies with prolonged follow-up. Mizandari performed the first human application of percutaneous RFA and showed no significant complications with a median survival of 89.5 days and median stent patency of 84.5 days. Only one case of stent obstruction was found 42 days after intervention.<sup>82</sup> Li et al demonstrated that stent patency did not significantly differ between RFA and non-RFA groups at 3 months, but stent patency was higher in the RFA group 9/11 (82%) of patients compared with non-RFA group 5/14 (36%) patients at 9 months.<sup>83</sup> In another published series comparing 18 patients who underwent RFA before stent placement to 18 patients who underwent stenting without RFA, the RFA group showed longer median stent patency times 5.8 months compared with control 4.5 months.<sup>84</sup> There was no significant difference in survival times between both the groups.

Though these novel studies have employed the prophylactic use of RFA to increase stent patency, RFA has also been utilized to obtain repatency once stent occlusion has already occurred. In a prospective study of nine patients with blocked metal stents, all patients had stent patency restored without the use of secondary stents.<sup>85</sup> Similarly, in a retrospective study of 14 patients with occluded stents, application of intraductal RFA resulted in stent repatency in all patients.<sup>86</sup>

## Photodynamic Therapy

Photodynamic therapy (PDT) is a technique that induces tumor necrosis and apoptosis by free radical induction. PDT has mostly been used for nonmelanotic skin lesions. In 1991 McCaughan et al described its use to treat unresectable cholangiocarcinoma in a patient who survived 4 years after treatment.<sup>87</sup> In PDT, a systemic photosensitizing agent using a hematoporphyrin derivative or dihematoporphyrin ether is administered to a patient and concentrates within the tissue with rapid turnover such as malignant cells. When exposed to a nonthermal light, a photochemical reaction occurs leading to free radical development. Aside from apoptosis induction, PDT

has also been described to have antiangiogenic and immune-inducing effects.<sup>88,89</sup> Complications include cholangitis and skin photosensitivity reaction. PDT has also been utilized as an adjunct with biliary stenting. The first randomized controlled trial of PDT with and without bile duct stenting showed improvement in bilirubin obstruction after PDT and not stenting alone.<sup>90</sup> Two subsequent meta-analyses demonstrated that PDT is associated with increased survival benefit, improved biliary drainage and better quality of life.<sup>91,92</sup> PDT is a safe and promising palliative treatment for cholangiocarcinoma; however, high-powered randomized controlled trials are needed to assess its efficacy further.

## Conclusion

Percutaneous intervention for MBO has exhibited tremendous evolution for treatment and management of MBO. Percutaneous biliary drainage and percutaneous cholecystostomy are foundational techniques for interventional management of MBOs. New stent designs, as well as their unique methods of deployment, have the potential to improve the quality of life of patients. Moreover, investigational techniques such as intraluminal brachytherapy, RFA, and PDT users are exciting new techniques that may extend the frontiers of biliary intervention that may lead to better patient care.

### Conflict of Interest

None.

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