4 Endoscopic and Percutaneous Biliary Drainage Procedures: Role in Preoperative Management, Diagnosis, and Palliation

Milton T. Smith

Introduction

Biliary drainage procedures for management of obstructive jaundice secondary to pancreatic cancer are frequently performed in clinical practice. Pancreatic cancer accounts for approximately 3 % of all cancers seen in the USA, and it is estimated that approximately 48,960 new cases will be seen in the USA in 2015 with 40,560 deaths [1]. This potentially fatal disease accounts for about 7 % of cancer deaths and is the fourth leading cause of cancer-related deaths among men and women [2].

Patients with pancreatic cancer often present with biliary obstruction as approximately 80 % of these neoplasms occur in the head of the gland. Jaundice, with or without pain, is seen in over half of patients who present with resectable, borderline resectable, or locally advanced disease [3, 4]. In other patients, jaundice develops later in the course as the disease progresses. Jaundice is typically a late finding when the primary tumor is located in the tail of the pancreas and often reflects metastatic disease. Surgical resection offers the only potential for curative treatment. However, only 15–30 % of patients are candidates for curative-intent surgery as the majority present at a more advanced stage and have either locally advanced or metastatic disease.

Obstructive jaundice may result in severe pruritus, progressive hepatocellular dysfunction, coagulopathy, malabsorption, and cholangitis [5]. Biliary decompression may be accomplished by surgical, radiologic, or endoscopic techniques. Although these modalities are equally effective in relieving biliary obstruction, endoscopic drainage via placement of a biliary stent (plastic or metal) during ERCP is generally considered safer, less invasive, and is preferred for most patients when technically feasible [6, 7]. PBD has been advocated largely in an attempt to reduce postoperative complications following surgical resections. This is based upon the rationale that pathophysiological derangements seen in the setting of biliary obstruction could potentially be reversed by restoring bile flow and ultimately translate into improved clinical outcomes.

Despite the fact that endoscopic and percutaneous drainage procedures are technically successful in 90–95 % of cases [5], the role of PBD remains controversial. Clinical studies have reported both beneficial and adverse effects, and most studies have advised against routine PBD due to the potential for procedure-related complications such as bleeding, perforation, pancreatitis, bacterial colonization of bile, and complications of stent

M.T. Smith, M.D. (✉)
Division of Digestive Diseases, University of Cincinnati, 231 Albert Sabin Way, ML #0595, Cincinnati, OH 45267, USA
e-mail: milton.smith@uc.edu

M.H.G. Katz, S.A. Ahmad (eds.), *Multimodality Management of Borderline Resectable Pancreatic Cancer*, DOI 10.1007/978-3-319-22780-1_4

occlusion such as cholangitis. Nevertheless, PBD is often considered necessary in clinical practice for selected patients. Most clinicians recommend PBD for the following clinical scenarios: (1) Patients with resectable disease who have surgery delayed for logistical reasons, (2) The resectability status may not be known with certainty at the time of initial ERCP, (3) To facilitate neoadjuvant chemoradiation in patients with borderline resectable cancer, (4) Management of cholangitis (or severe pruritus), (5) Palliation of jaundice in patients with unresectable disease. This chapter will focus on biliary drainage procedures and their role in management, diagnosis, and palliation of patients with obstructive jaundice due to pancreatic cancer.

Role of ERCP in the Diagnosis of Pancreatic Cancer

ERCP is a highly sensitive modality for visualization of the biliary tree and pancreatic ducts. It also provides the opportunity to obtain tissue samples and perform therapeutic maneuvers. However, with advances in cross-sectional imaging and endoscopic ultrasound (EUS), the role of ERCP in patients with suspected pancreatic cancer has evolved into a mainly therapeutic modality for patients with biliary obstruction and require decompression. ERCP alone provides little staging information for pancreatic cancer.

Certain endoscopic and radiographic features observed during ERCP should alert the endoscopist to the possibility of pancreatic cancer. The presence of mucus extrusion from the papillary orifice is compatible with a main duct intraductal papillary mucinous neoplasm (IPMN), a condition that may lead to the development of pancreatic ductal adenocarcinoma. The pancreatogram in such cases might also reveal intraductal mucin which is seen as a filling defect within the pancreatic duct (Fig. 4.1). Direct invasion of the ampulla or duodenal wall caused by a neoplasm in the head of the pancreas is sometimes seen endoscopically. Standard forceps biopsies may yield a diagnosis in these cases (Fig. 4.2). Mass lesions in the head of the pancreas often cause simultaneous obstruction of the common duct and pancreatic duct (i.e., double-duct sign). At ERCP, this appears as a focal stricture of the common bile duct and pancreatic duct, typically

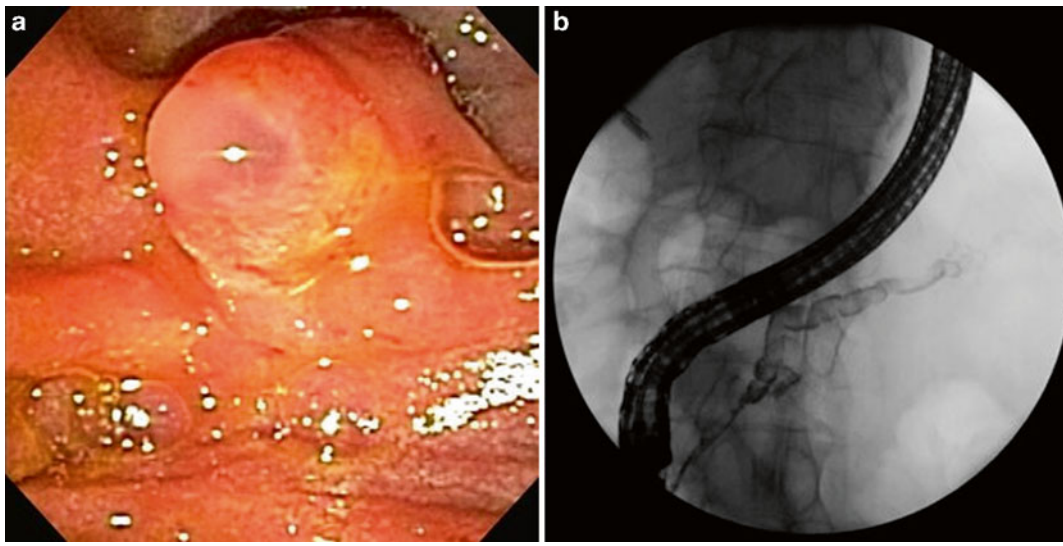

Fig. 4.1 (**a**) Endoscopic photograph of thick mucus extruding from the orifice of the major papilla. This finding is compatible with main-duct intraductal papillary neoplasm, a condition strongly associated with pancreatic ductal adenocarcinoma. (**b**) Pancreatogram revealing a long cast-like filling defect in the main pancreatic duct, reflecting the presence of intraductal mucus. Also note the presence of a ductal stricture in the head of the pancreas

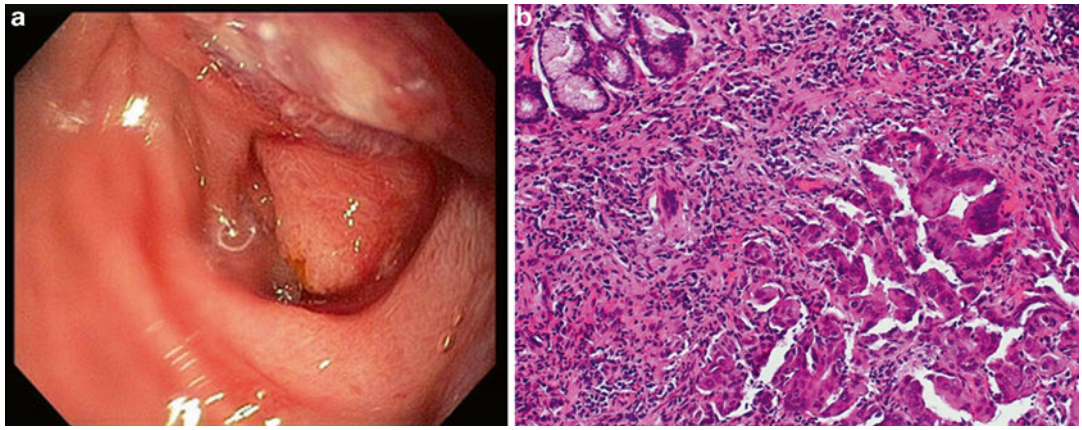

Fig. 4.2 (**a**) Endoscopic photograph of direct invasion of the duodenal wall caused by a pancreatic head mass. Note the uninvolved orifice of the major papilla seen downstream. (**b**) Standard forceps biopsies confirmed adenocarcinoma invading the duodenal wall

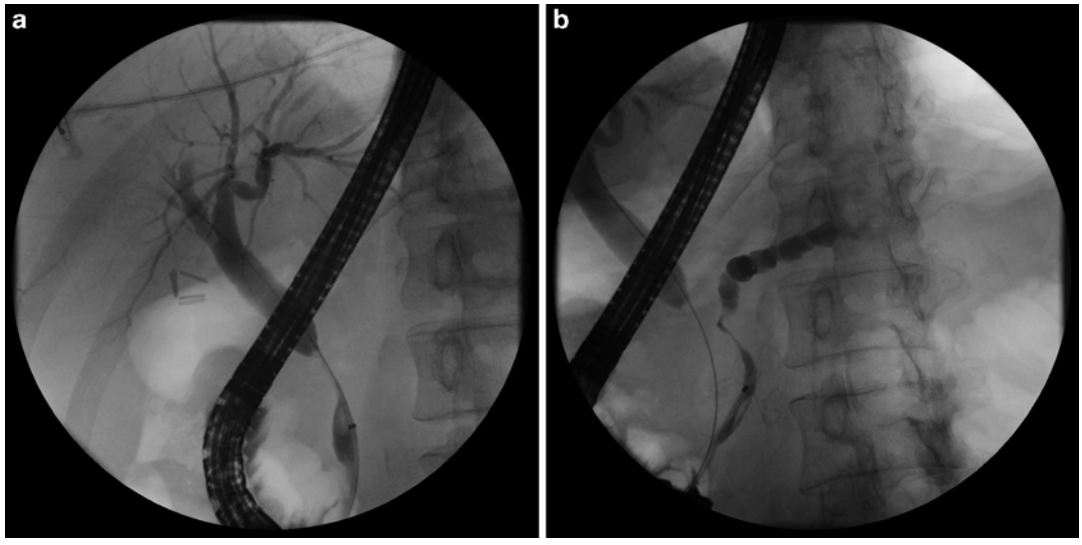

Fig. 4.3 (**a**) Double-duct sign. Cholangiogram revealing a common bile duct stricture with upstream dilation. (**b**) Pancreatogram revealing a long irregular stricture in the head of the pancreas with upstream dilation. Simultaneous obstruction of the common duct and pancreatic duct is highly suggestive of a mass lesion in the head of the pancreas

with associated upstream dilation of both ducts (Fig. 4.3). Other features of a stricture which are suggestive of malignancy include an abrupt cut-off of the pancreatic duct, a ragged contour, or stricture length >1 cm. These radiographic features are helpful but nondiagnostic and may occasionally be found in benign conditions such as chronic pancreatitis. The presence of a stricture in the pancreatic duct and/or bile duct must be interpreted in clinical context, but generally leads to tissue sampling during ERCP if the diagnosis remains in question as a definitive diagnosis of malignancy requires tissue confirmation.

Tissue sampling techniques during ERCP include brush cytology, forceps biopsy, aspiration of bile or pancreatic juice for cytology, or a

combination. In patients in whom a plastic stent has already been placed, the stent can be spun and the cells obtained can be evaluated [8]. Exfoliated malignant cells may be adherent to the surface of the stent as they become entrapped within biofilm and sludge. The sensitivity rate for ERCP-directed brush cytology or biopsy is 30–50 %, with a combination of techniques achieving sensitivity rates of approximately 70 % [9, 10]. This is considerably less than EUS-guided fine needle aspiration (FNA) which has a sensitivity of approximately 85–90 % for the diagnosis of pancreatic cancer [11]. Several studies have shown that diagnostic yield during ERCP can be increased by using a combination of different tissue sampling methods [12, 13]. Unfortunately, the negative predictive value in tissue sampling during ERCP using a combination of techniques is nearly 40 % [12].

Although aspiration of bile or pancreatic juice is simple to perform, fluid cytology alone has a low sensitivity and is not performed by most endoscopists. Fluid specimens are often acellular, likely due to the desmoplastic nature of certain tumors or failure to invade the ductal epithelium. Techniques to increase tumor exfoliation prior to collecting specimens, such as stricture dilation or saline irrigation, have not demonstrated increased cancer detection rates in prospective comparative trials [12]. Forceps biopsies have a higher yield, but generally require a sphincterotomy to gain access to the bile duct or pancreas. When performing forceps biopsies, it may be helpful to first place a guidewire across the stricture to maintain access and for use as a guide for cannulation and positioning of the biopsy forceps (Fig. 4.4). Performing intraluminal forceps biopsies during ERCP can be technically challenging as the device cannot be passed over a guidewire. It may also increase the risks of the procedure, including bleeding, pancreatitis, and perforation. By comparison, biliary brush cytology is relatively easy to perform as the brush passes over a prepositioned guidewire to acquire a specimen within the stricture. The overall technical success rate of biliary brush cytology is >90 %. Brush cytology in the pancreatic duct is sometimes helpful but is frequently more difficult to perform. Pancreatic cancer often causes tight strictures of the main pancreatic duct which prohibit passage of the brush through the tumor in greater than 25 % of patients [12] (Fig. 4.4). Because of the aforementioned challenges, most practitioners perform biliary brush cytology alone, which has sensitivity as low as 30 %. Although the sensitivity of brush cytology or forceps biopsy alone is suboptimal, both techniques are almost 100 % specific [13]. Advanced techniques such as digital image analysis may enhance the accuracy of routine cytology [14], but is not widely available. Additional methods to improve the diagnostic yield such as the molecular analysis of the components of pancreatic juice and bile remain experimental [9, 15, 16]. Although the overall performance of tissue sampling techniques during ERCP in patients with suspected pancreatic cancer is significantly lower than EUS-FNA, it remains an important modality and should be performed whenever a diagnosis has not been established at the time of the procedure.

Rationale for Preoperative Biliary Drainage

Historically, major hepatobiliary surgical procedures in patients with obstructive jaundice have been associated with significant morbidity and mortality, largely due to the development of postoperative complications such as sepsis, bleeding disorders, and renal failure. Biliary obstruction has been regarded as a risk factor that can worsen the outcome after surgery [17]. The primary rationale of PBD for patients with biliary obstruction due to pancreatic cancer is to reduce the risk of postoperative complications. The concept of PBD was introduced by A.O. Whipple and colleagues in 1935 when they published one of the first case series of PBD for patients with periampullary cancer [18]. The two-staged technique involved performing a preliminary open biliary diversion procedure (cholecystogastrostomy) to reduce jaundice, followed by resection of the primary tumor at a later stage, depending on the severity of jaundice. The goal of this approach was to optimize the overall physical status of the patient prior to definitive resection.

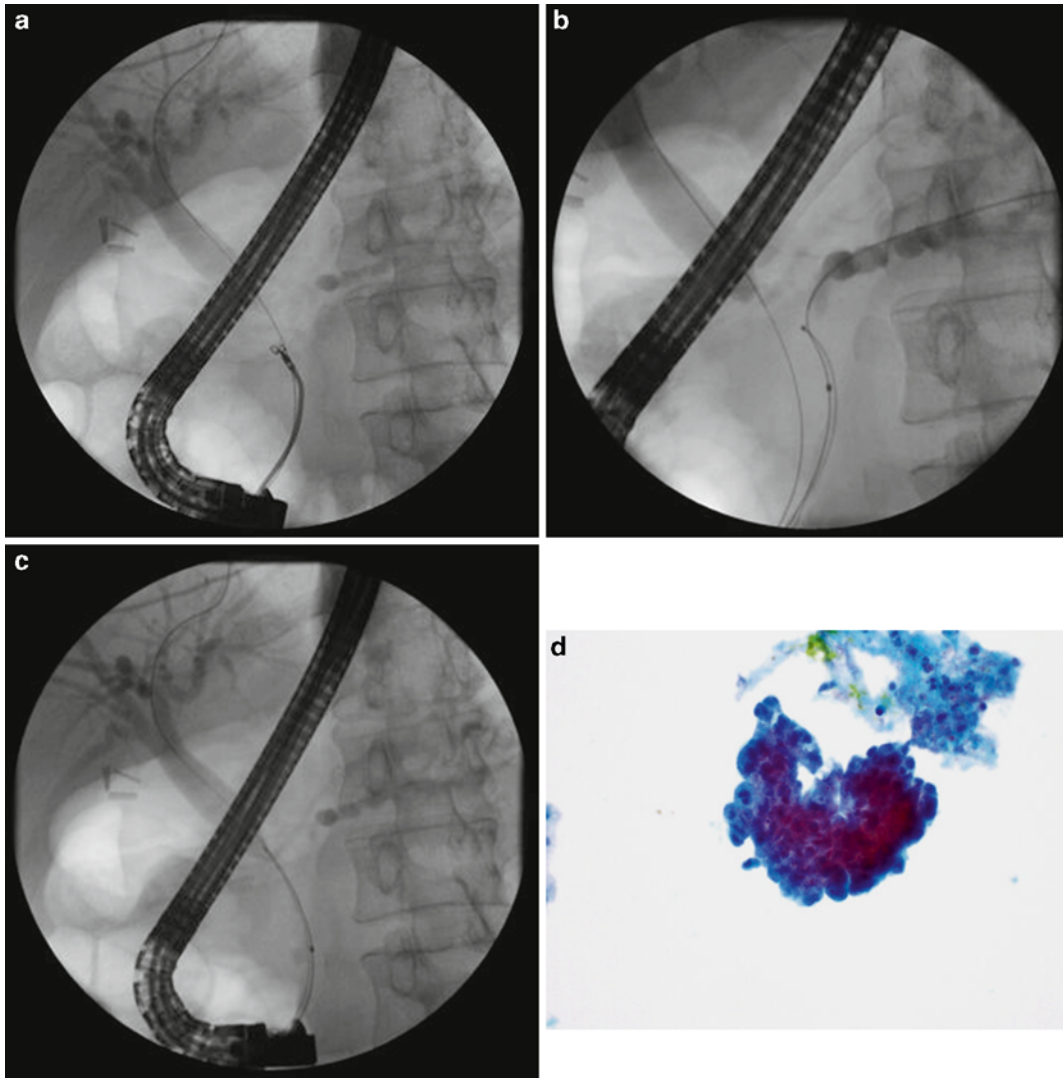

Fig. 4.4 (**a**) Biliary forceps biopsy. A guidewire passed through the biliary stricture is used as a guide for cannulation and positioning of the biopsy forceps. (**b**) Pancreatic duct brush cytology. A second guidewire has been passed through the pancreatic duct stricture and is used to position the cytology brush. Brushings within pancreatic duct may be challenging to perform due to the tight nature of the stricture. (**c**) Biliary brush cytology. A cytology brush has been passed over a prepositioned guidewire to acquire a specimen within the stricture. (**d**) Photomicrograph of a specimen obtained during biliary brush cytology revealing crowding and overlapping of cells, compatible with adenocarcinoma

Biliary obstruction is associated with several deleterious effects. Animal studies have shown that obstructive jaundice leads to a proinflammatory state resulting from portal and systemic endotoxemia [19]. Decreased bile in the intestinal lumen causes increased permeability of the intestinal mucosal barrier, promoting bacterial translocation and the occurrence of endotoxemia [20]. Systemic endotoxemia leads to impaired cellular immunity and increased concentrations of proinflammatory cytokines such as interleukin-6 (IL-6), interleukin-10 (IL-10), interleukin-8 (IL-8), and tumor necrosis factor (TNF) [21–23]. The overall effects of obstructive jaundice in

humans on endotoxin and cytokines may be different from those seen in animal models [24]. Biliary obstruction also causes a reduction in hepatic reticuloendothelial system function leading to a diminished clearance of endotoxin by Kupffer cells [24, 25]. Persistent elevation of cytokines has been associated with protein calorie depletion, a factor associated with higher surgical complications which could potentially be reversed by biliary decompression. Malignant biliary obstruction may also adversely affect coagulation due to bile acid-induced hepatocyte damage [26] as well as impaired hepatic synthesis of vitamin K-dependent coagulation factors secondary to reduced vitamin K absorption from the intestine. Despite these effects favoring bleeding complications, a recent study has shown that patients with severe biliary obstruction may also develop a procoagulant state which was almost completely reversed by preoperative endoscopic biliary drainage [27]. In addition to impairment of immune function and coagulopathy, biliary obstruction is also associated with renal dysfunction. Cholestatic jaundice is known to have deleterious effects on cardiovascular function, blood volume, and vascular reactivity. The overall effect of obstructive jaundice predisposes the kidney to prerenal failure and acute tubular necrosis. Most evidence suggests that the constituents of bile (cholesterol, bilirubin, bile acids) do not exert a direct nephrotoxic effect [28]. A multivariate analysis has shown that renal dysfunction in patients with obstructive jaundice is associated with the degree of biliary obstruction as well as the age of the patient [29]. Biliary obstruction may also be associated with impaired myocardial function and is associated with increased plasma levels of atrial natriuretic peptide (ANP). Internal biliary drainage results in improvement in cardiac function and normalization of ANP [30].

The adverse effects of biliary obstruction on multiple organ systems and immune function may adversely impact the outcome after major surgery for patients with pancreas cancer. Preoperative biliary drainage has the potential to improve surgical outcomes by reversing the detrimental effects via restoration of bile flow.

Methods of Preoperative Biliary Drainage

Endoscopic stent placement and percutaneous biliary drainage have largely replaced surgical biliary bypass for management of biliary obstruction due to pancreatic cancer. These techniques are generally considered less invasive, less expensive, and have a shorter recovery time as compared to surgical procedures. The choice between endoscopic vs. percutaneous biliary drainage is often a matter of a local expertise and patient anatomy, although endoscopic stent placement is preferred whenever possible due to fewer procedure-associated complications [31]. Percutaneous biliary drainage is more often used when endoscopic stent placement is unsuccessful or not technically possible due to altered anatomy (e.g., duodenal obstruction, tumor invasion of the ampulla, or previous surgical bypass procedures).

Percutaneous Biliary Drainage

Percutaneous transhepatic biliary drainage (PTBD) was introduced in the 1960s and was the treatment of choice for biliary drainage for over two decades [32, 33]. PTBD drainage is most often performed using fluoroscopic guidance although ultrasound can be helpful for the initial puncture when the bile ducts are dilated [34]. The technique involves passing a skinny needle (21 or 22 gauge) through the hepatic parenchyma until reaching a dilated intrahepatic bile duct. A percutaneous cholangiogram is performed by injecting contrast as the needle is slowly withdrawn, followed by passage of a small diameter (0.018 in.) guidewire to secure the position in the biliary tree. Once the dilated duct has been accessed with the needle, the needle is exchanged for a coaxial system to upsize the 0.018-in. access guidewire to a larger guidewire (e.g., 0.035 or 0.038 in.) which is more stable and can be used for further interventions.

PTBD can provide biliary drainage in three ways. The simplest of these is external drainage which involves decompressing the biliary tree through a percutaneous tube which exits the skin,

but the intraductal tip is left upstream to the site of biliary obstruction. The method is typically used when a tight stricture cannot be traversed with a guidewire after percutaneous access to the biliary tree has been achieved. A major disadvantage of external drainage is the fact that bile flow to the duodenum is not restored. For internal–external drainage, a directional catheter is inserted through the percutaneous sheath and advanced over a hydrophilic guidewire through the biliary obstruction and into the duodenum. The catheter can then be exchanged over a stiffer guidewire (e.g., Amplatz) for a multiside-hole drainage catheter which is passed through the stricture into the duodenum. The internal–external catheter allows bile to drain externally into a bag and/or internally into the duodenum, thereby preserving the normal enterohepatic circulation of bile (Fig. 4.5). The third technique establishes internal drainage by percutaneous placement of a plastic or self-expandable metal stent (SEMS) across the biliary stricture. Recent studies have shown percutaneous SEMS placement to be a safe and effective technique [35–38]. Although it is common practice to establish initial internal–external drainage prior to SEMS placement, some experienced centers have reported good results with percutaneous SEMS insertion as a single-stage procedure [35, 36]. A retrospective study from the UK reported an overall technical success rate of 79 % among 67 patients undergoing percutaneous short SEMS placement for biliary obstruction due to pancreatic or periampullary tumors [35]. The complication rate was 9.4 % although all complications were managed conservatively and none precluded subsequent surgery.

One disadvantage of PTBD is that it cannot be used in the presence of moderate or severe ascites [39]. PTBDs can be cumbersome for patients to manage and require significant maintenance. External drains require periodic emptying, flushing of the drain, and drain exchanges to prevent occlusion [40]. PTBDs can also be prone to leakage, dislodgement, and complications such as hemobilia and infection. A recent prospective study involving 109 patients with advanced malignancy showed that PTBD improved pruritus and hyperbilirubinemia, but not overall quality of life [41]. Despite potential drawbacks, PTBD continues to have an important role for management of biliary obstruction, especially when ERCP is unsuccessful [42].

Endoscopic Biliary Drainage

The most common and generally preferred method of achieving preoperative biliary drainage is by ERCP with stent placement. Endoscopic stents are often used as a bridge to surgery for patients with resectable or borderline resectable disease as well as for long-term palliation for unresectable pancreatic cancer. The main advantage of an endoscopic approach over PTBD is the avoidance of skin and liver punctures as well as the risk of tumor seeding which may occur along the catheter and to the skin [43]. Recent meta-analyses have suggested that endoscopic stenting provides superior results to open surgical bypass in patients with distal biliary obstruction due to pancreatic cancer [7, 44]. Biliary drainage may be achieved using either plastic stents or SEMS and it is now clear that stent luminal diameter is a critical factor for both types as the risk of stent occlusion correlates with stent diameter. In general, wider diameter stents have a lower risk of short-term occlusion, whether plastic or metal.

Plastic biliary stents have been used since their development in the 1980s and are now commercially available in a wide variety of diameters, lengths, and designs (Fig. 4.6). They may be composed of various materials including polyethylene, polyurethane, and Teflon. Plastic biliary stents are available in diameters ranging from 5 to 12 Fr and lengths from 1 to 18 cm [45]. The primary advantages of using plastic stents for malignant biliary obstruction are that they are effective, have lower costs, and are easily removed or exchanged. Plastic stents are often selected when a diagnosis has not been established or the patient's resectability status is unknown at the time of initial endoscopic treatment. The major disadvantage of plastic stents is that they have a high rate of occlusion due to formation of bacterial biofilm, sludge, as well as dietary fibers [46] (Fig. 4.7); this leads to the

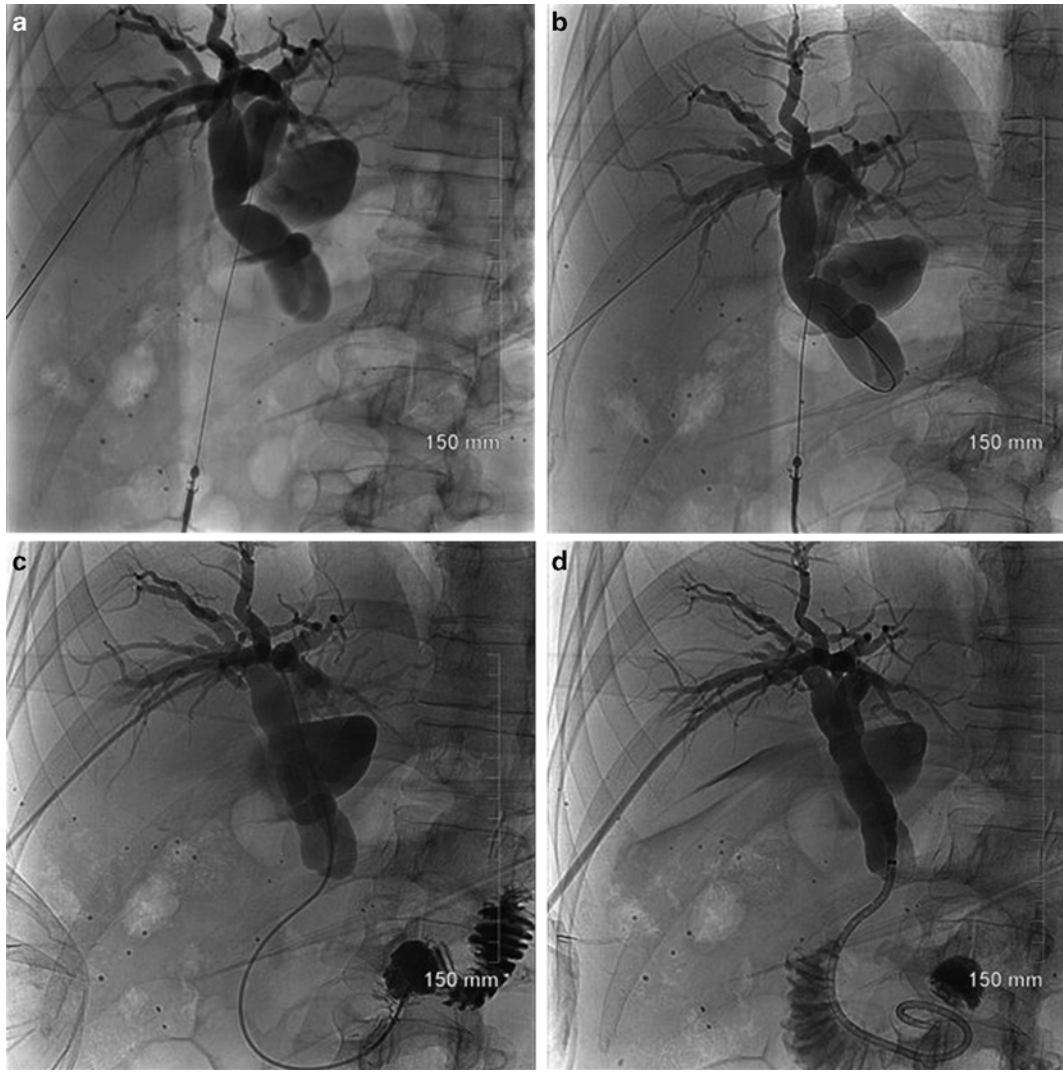

Fig. 4.5 (**a**) The patient is a 60-year-old male with borderline resectable pancreatic head cancer who underwent unsuccessful ERCP due to failed bile duct cannulation. A percutaneous transhepatic cholangiogram was performed by injection of contrast through a 22 gauge Chiba needle. Needles are shown entering left and right intrahepatic ducts. (**b**) Initial attempts to pass a guidewire through the high-grade bile duct stricture in the head of the pancreas were unsuccessful. No contrast flowed through the stricture. (**c**) A stiff 0.035 in. hydrophilic guidewire and 5 Fr catheter were ultimately passed through the stricture into the duodenum. (**d**) Following placement of a 0.035 Amplatz guidewire and dilation of the tract to 10 Fr, a 10 Fr multiside hole internal-external drainage catheter was placed with tip reaching the transverse duodenum

need for repeat procedures and stents exchanges. In general, 7 Fr plastic stents remain patent for approximately 8 weeks whereas 10 Fr plastic stents remain patent for an average of 3–5 months [47]. It is important to note that plastic biliary stents often do not maintain patency during the time required for most patients to complete neoadjuvant chemoradiotherapy for pancreatic cancer. A recent retrospective study reported that among 49 patients treated with plastic stents who were undergoing neoadjuvant therapy, 55 % required repeat ERCP for stent malfunction at a median of 82.5 days after initial stent placement [48]. Studies evaluating stent designs have

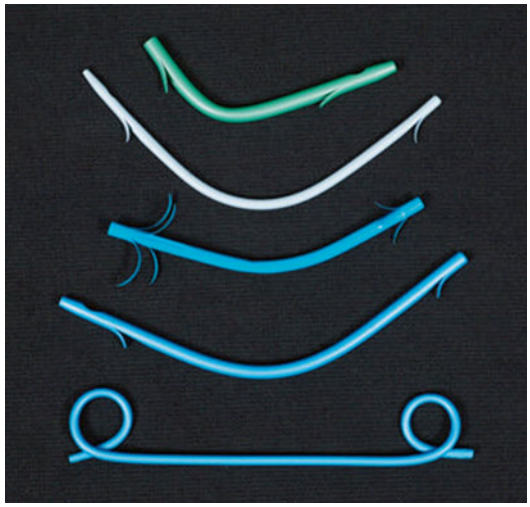

Fig. 4.6 Various plastic biliary stents. Plastic stents are available in a variety of diameters, lengths, and designs and may be composed of different materials. Stents which have a wider luminal diameter generally remain patent longer

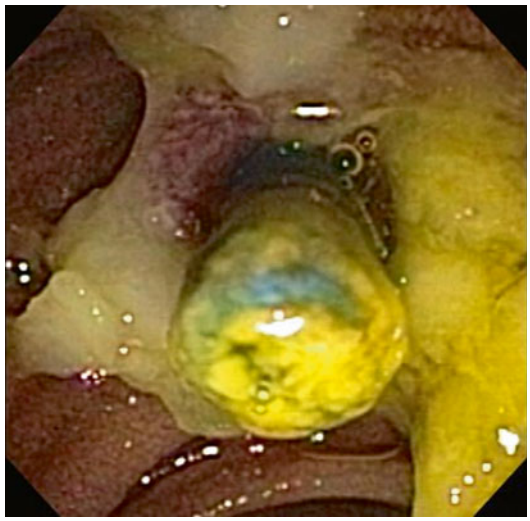

Fig. 4.7 Endoscopic photograph of an occluded plastic biliary stent. Plastic stents occlude due to the formation of bacterial biofilm and biliary sludge. High occlusion rates is a limiting factor in the use of plastic stents for preoperative biliary decompression for pancreatic cancer

compared stents composed of Teflon without side holes to standard polyethylene stents with side holes. No difference in patency rates was found based upon stent composition or design [49, 50]. Although it is generally accepted that larger diameter plastic stents (10 Fr or greater) have a longer patency than smaller diameter stents, a study comparing 10–11.5 Fr stents found no difference in patency rates [51]. A Cochrane meta-analysis found that choleretic agents such as ursodeoxycholic acid (UDCA) and/or antibiotics do not appear to improve plastic stent patency rates [52].

SEMS are now widely used for management of malignant biliary obstruction. As with plastic stents, SEMS are available in a variety sizes and designs (Fig. 4.8). Multiple studies have shown that when compared to plastic stents, SEMS have a superior patency rate when used for preoperative biliary decompression due to pancreatic cancer [7, 48, 53–58] (Fig. 4.9). The improved patency of SEMS relates to the fact that when fully deployed, SEMS have a roughly threefold wider luminal diameter than most plastic stents. Longer stent patency is especially important as more centers adopt neoadjuvant therapy as a standard of preoperative care. Stent occlusions during this period can result in severe complications such as cholangitis as well as interruptions in therapy, hospitalizations, unplanned procedures, and delays in eventual surgery [59]. In a recent prospective study evaluating SEMS in 55 patients undergoing neoadjuvant therapy for pancreatic cancer, only 15 % experienced stents malfunctioned by 260 days after placement [60]. This compares favorably to a 55 % stent malfunction rate when plastic stents were used for a similar patient population [48]. Another retrospective study evaluating plastic stents and SEMS for preoperative biliary decompression reported a 39 % stent dysfunction rate for those who received plastic stents compared to no stent dysfunction for those who received an SEMS [54]. Adams et al. evaluated stent complications among 52 patients who underwent placement of either a plastic stent or SEMS to receive neoadjuvant therapy for pancreatic cancer [57]. The complication rate was nearly seven times higher with plastic stents than with SEMS. Moreover, the rate of hospitalization for stent-related complications was threefold higher in the plastic stent group than the SEMS group.

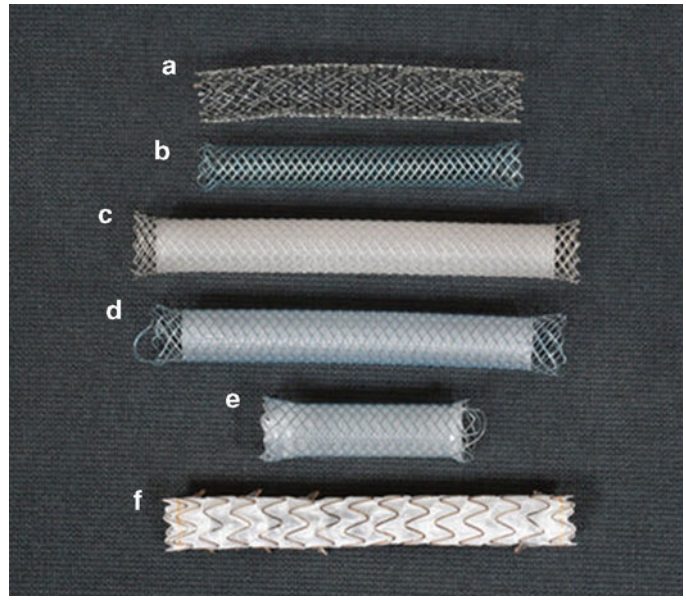

Fig. 4.8 Various self-expandable metal biliary stents. (**a**) Uncovered Zilver (Cook) (**b**) uncovered Wallflex (Boston Scientific) (**c**) partially covered Wallstent (Boston Scientific) (**d**) partially covered Wallflex (Boston Scientific) (**e**) fully covered Wallflex (Boston Scientific) (**f**) fully covered Viabil (ConMed)

One factor that led to the initial use of plastic stents for preoperative biliary decompression was the concern that uncovered SEMS could potentially cause technical difficulties with transecting the bile duct and creating a biliary anastomosis during subsequent pancreaticoduodenectomy. Studies have now shown that placement of a short-length SEMS (typically 4–6 cm length) does not interfere with the outcome of surgery [5, 54, 61–63]. Siddiqui et al. reported the outcome of 241 patients with resectable or borderline resectable disease who underwent preoperative SEMS placement [63]. Uncovered, partially covered, and fully covered SEMS were used. Ultimately, 166 patients underwent curative-intent surgery without any observed technical difficulties during surgery due to the presence of an SEMS. Similarly, Mullen et al. found no difference in intraoperative or postoperative complications, or length of hospital stay among 29 patients who underwent pancreaticoduodenectomy after SEMS placement compared to those who had plastic stents (n-141), no stent (n-92), or biliary bypass (n-10) prior to surgery [64]. It is advisable during stent placement to use the shortest length SEMS possible to bridge the stricture with care taken to leave an adequate length of common hepatic duct un-stented (ideally 2 cm) to simplify any future surgical anastomosis, especially if using an uncovered SEMS. The choice between plastic stent vs. SEMS may ultimately rely on other factors such as cost, expected survival length, and certainty of diagnosis at the time of initial ERCP.

Although SEMS remain patent longer than plastic stents, they are also at risk for occlusion due to tumor ingrowth through the mesh interstices, overgrowth beyond the ends of the stent, or due to a hyperplastic response of normal tissue caused by the stent (Fig. 4.10). For this reason, SEMS were developed which are partially or fully covered with a goal of improving patency by preventing tumor and tissue ingrowth. Coverings include material made of polytetrafluoroethylene (PTFE), expanded polytetrafluoroethylene/fluorinated ethylene propylene (ePTFE/FEP), or silicone membranes. The covering may be on the exterior or interior of the stent. Some fully covered stents have fenestrations in the cover without exposing the metal wires. Unfortunately, covered stents may also occlude due to stent migration, tumor/tissue overgrowth, tumor ingrowth as the covering deteriorates over time, or possibly due to food debris [40]. Reflux of duodenal contents into SEMS is also known to occur [65] and could potentially cause problems

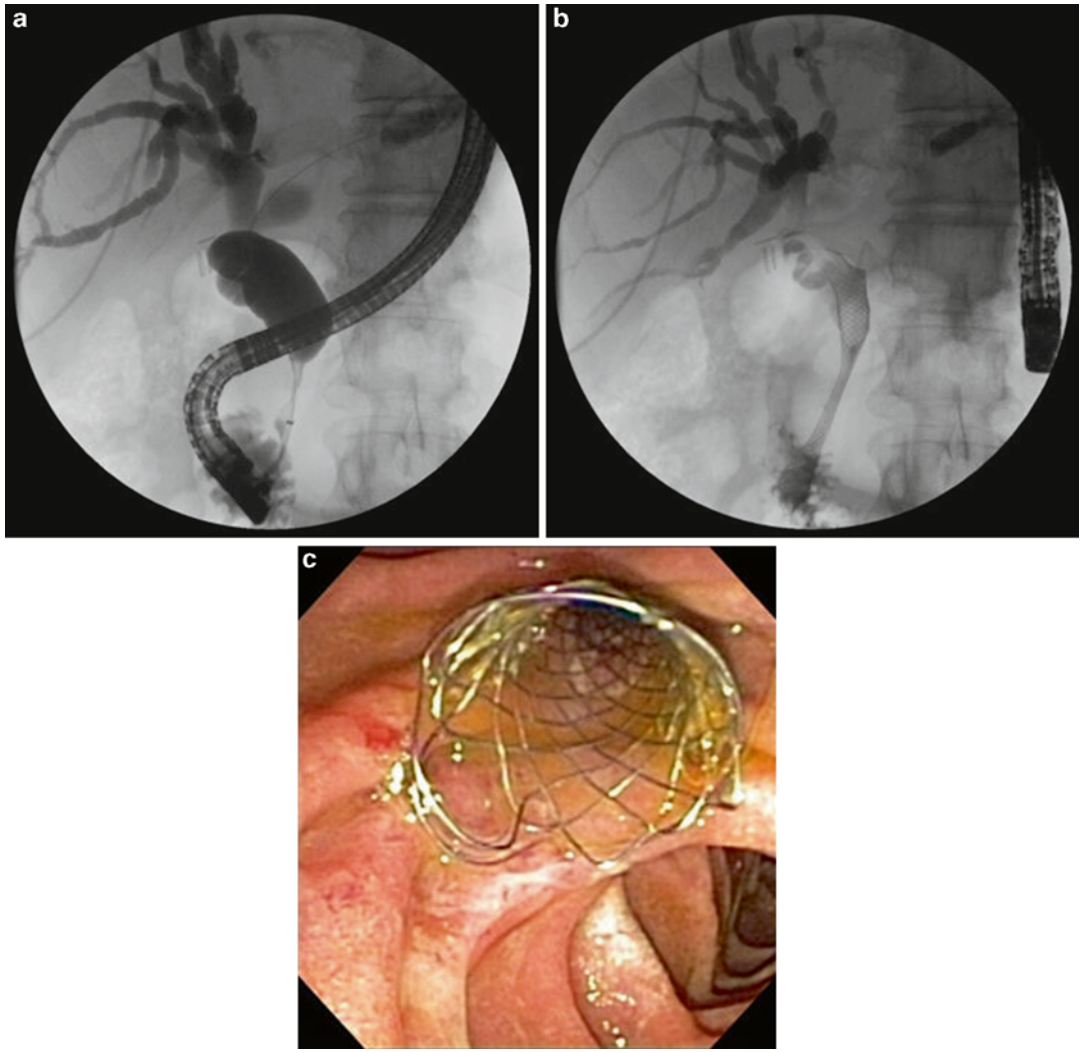

Fig. 4.9 (**a**) A patient with borderline resectable pancreatic cancer underwent ERCP for management of obstructive jaundice prior to neoadjuvant therapy. The cholangiogram revealed a distal common bile duct stricture with upstream dilation. (**b**) A 10×60 mm biliary self-expandable metal stent was placed with subsequent resolution of jaundice. (**c**) Endophoto of a biliary self-expandable metal stent following placement

in some patients. One of the advantages of uncovered SEMS, which has been shown in several studies, is their low migration rate (0–2 %) [56, 66, 67]. This is presumably due to embedding of the stent into the wall of the bile duct after deployment. Covered SEMS have a higher migration rate of approximately 6–8 %. Partially and fully covered stents have the advantage that they can be repositioned or fully removed using a rat-tooth forceps or snare [45]. SEMS are available in 6, 8, and 10 mm diameters when fully deployed, which is a key feature in determining the risk of occlusion. A large prospective multicenter study randomized 241 patients with malignant biliary strictures to receive uncovered SEMS of different designs in two diameters (i.e., 6 mm Zilver, 10 mm Zilver, or 10 mm Wallflex). SEMS occlusions were much more frequent with a 6-mm diameter SEMS and equivalent in the two 10-mm arms despite major differences in stent design, material, and expansion, suggesting that diameter is the critical feature [68]. Similarly, Yang et al.

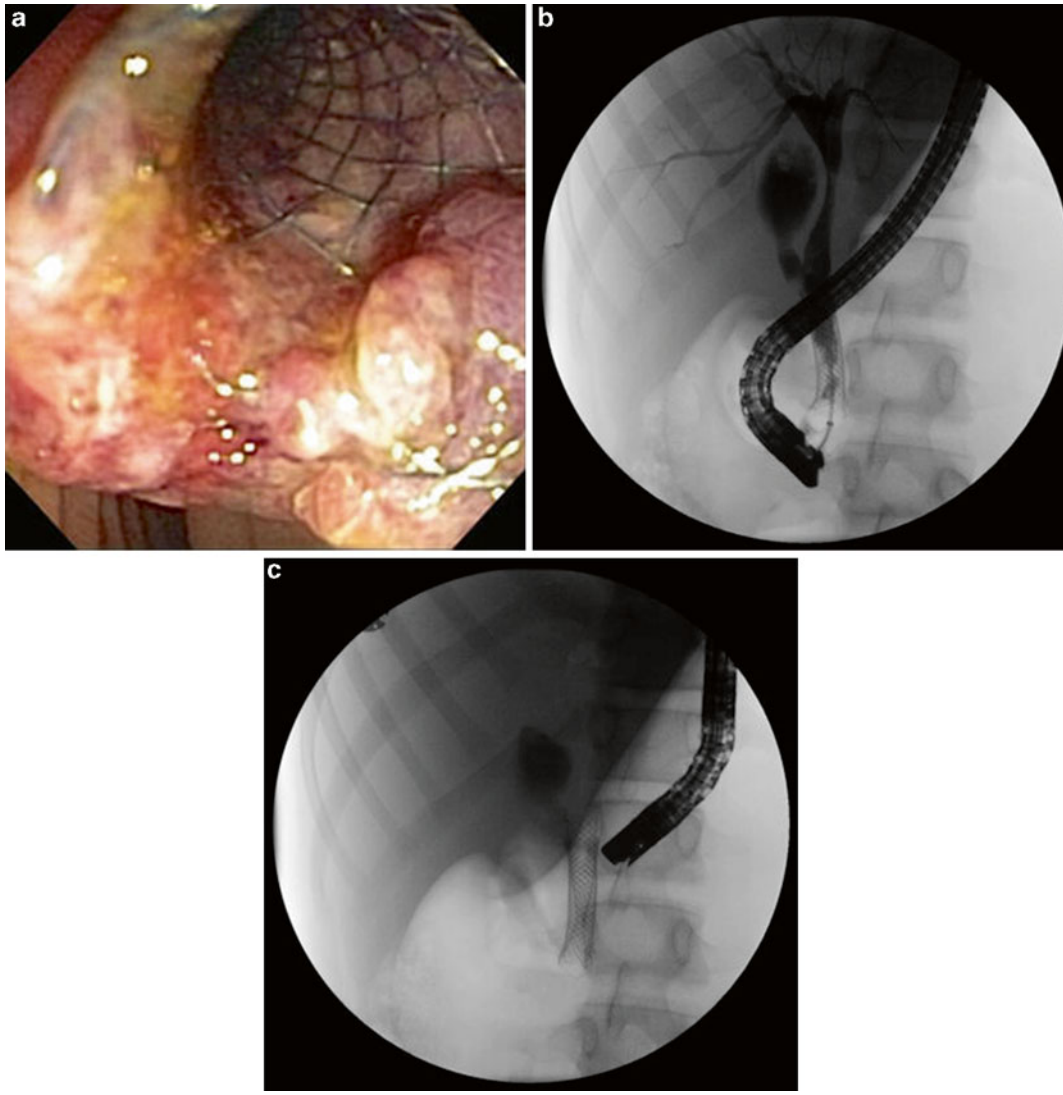

Fig. 4.10 (**a**) Endoscopic photograph demonstrating tissue overgrowth at the duodenal end of a biliary self-expandable metal stent. (**b**) Balloon occlusion cholangiogram revealing a biliary stricture caused by tumor or tissue ingrowth through the interstices of the existing metal biliary stent. (**c**) A second SEMS was deployed within the existing SEMS with resolution of biliary obstruction

showed no significant difference in the rate of occlusion when using uncovered SEMS of equal diameter, but different stent design [69].

Studies comparing the differences in patency rates between covered and uncovered SEMS in patients with malignant distal bile duct obstruction have shown conflicting results. For example, two randomized multicenter trials found no difference in patency rates [70, 71]. Another randomized trial showed longer patency with covered SEMS [72]. A meta-analysis concluded that covered SEMS have a significantly longer patency compared with uncovered SEMS [73]. However, a subsequent meta-analysis found no difference in patency between covered and uncovered SEMS at 6 and 12 months, although covered stents had a higher rate of stent migration [74].

Another concern for patients undergoing placement of a covered SEMS who have an intact

gallbladder is the potential for developing cholecystitis due to obstruction of the cystic duct origin. Although the rate of developing cholecystitis as a complication after SEMS placement has been low in most studies, rates of up to 10 % have been reported [75, 76]. Some endoscopists routinely perform a biliary endoscopic sphincterotomy (B-ES) to facilitate SEMS placement and to help avert the risk of pancreatitis due to SEMS occlusion of the pancreatic duct. On the other hand, B-ES may itself be a risk factor for procedure-related complications including pancreatitis, bleeding, perforation, and stent migration. Studies comparing the outcome of SEMS placement in patients with and without a preceding B-ES have shown the following: (1) SEMS (covered and uncovered) may be placed without a B-ES with very high success rates equal to those who underwent B-ES prior to stent placement, (2) Avoiding a B-ES prior to SEMS placement may reduce the risk of complications, especially short-term complications such as bleeding and perforation [77, 78].

EUS-Guided Biliary Drainage

Despite a success rate of >90 % in most reports, ERCP with stent placement for malignant biliary obstruction occasionally fails owing to anatomical or technical problems. Surgically altered anatomy, gastric outlet obstruction, tumor infiltration of the ampulla, and periampullary diverticula may result in inability to reach or visualize the ampulla during ERCP. PTBD or surgical interventions are conventionally performed after unsuccessful ERCP. EUS-guided biliary drainage (EUS-BD) has recently emerged as an effective biliary drainage technique in cases of unsuccessful ERCP. Following the first report of EUS-BD by Giovannini et al. in 2001 [79], many groups have subsequently reported on the efficacy of EUS-BD as an alternative biliary drainage modality after unsuccessful ERCP [80–88]. EUS-BD is accomplished using one of three techniques. Transluminal biliary drainage involves accessing the common duct or a dilated left intrahepatic duct under EUS guidance, followed by dilation of the tract and placement of a stent between the common duct and duodenum (cholecystoduodenostomy) or the stomach and a left hepatic lobe duct (hepaticogastrostomy). The stent drains the biliary tree into the GI tract without crossing the site of biliary obstruction. In the EUS-BD rendezvous procedure, the biliary tree is accessed via the common duct or a left hepatic lobe duct and a guidewire is passed via the bile duct across the papilla into the duodenum. The EUS-placed duodenal guidewire is then used to perform ERCP in the usual retrograde fashion. It should be noted that the EUS guided rendezvous technique is possible only when the papilla can be reached endoscopically. With the EUS-guided antegrade technique, transgastric puncture of a dilated intrahepatic duct is performed followed by tract dilation and transpapillary placement a stent across the level of obstruction in antegrade fashion. The antegrade technique may be useful when the papilla cannot be reached endoscopically. EUS-BD is a technically complex procedure requiring advanced skills in interventional EUS. The overall success and complication rates are approximately 81 % and 15 %, respectively, in expert hands [47].

Efficacy of Preoperative Biliary Drainage

The benefit of PBD prior to pancreaticoduodenectomy in patients with resectable pancreatic cancer remains controversial despite numerous studies which have addressed this issue. Although several studies have suggested more perioperative complications in patients who underwent PBD, this approach remains popular in clinical practice. A recent study found that the use of preoperative biliary stenting doubled between 1992 and 2007, with most patients undergoing stent placement prior to surgical consultation [89]. Another study which evaluated the current clinical practice in pancreatic cancer surgery at German community and university hospitals found that of 102 returned questionnaires, 54 % preferred preoperative drainage procedures for cholestasis [90].

Several meta-analyses have evaluated the impact of PBD on the surgical outcome of patients with malignant obstructive jaundice undergoing pancreaticoduodenectomy [91–98] (Table 4.1). A 2002 meta-analysis by Sewnath et al. included 5 randomized control trials (RCTs) and 18 retrospective studies (RS) published from 1966 to 2001 [94]. They found that patients who underwent PBD had significantly higher overall complications (mainly PBD-related), prolonged hospital stays, and no difference in mortality compared to patients who went directly to surgery. This data led to the conclusion that PBD carries no benefit and should not be performed routinely. A second meta-analysis published in the same year which included two RCTs and eight RS concluded that preoperative biliary stent placement had neither a positive or adverse effect on surgical outcomes for patients with pancreatic cancer [93]. Velanovich et al. evaluated 1 RCT and 15 cohort studies, concluding that PBD increased postoperative wound infections by about 5 % but did not promote or protect from other complications [95]. Similarly, Garcea et al. found that PBD significantly increases the rates of bile culture positivity for bacteria and the probability of wound infection [91]. Otherwise, no evidence was found that PBD directly increases morbidity and mortality. Another meta-analysis in 2011 which reviewed 14 RS found no difference in overall postoperative complications or mortality between patients with or without PBD [92]. The authors concluded that PBD should not be used routinely for malignant obstructive jaundice. Fang et al. published a Cochrane review in 2012 which updated their previous meta-analysis from 2008 [96, 97]. Six RCTs were evaluated with 520 patients randomized (PBD-265, no PBD-255). They found no difference in mortality, but significantly higher serious morbidity in the PBD group vs. the direct surgery group. The study concluded that there is not sufficient evidence to support or refute routine PBD for patients with obstructive jaundice. Finally, a recent meta-analysis published in 2014

Table 4.1 Summary of meta-analyses evaluating the impact of PBD for biliary obstruction prior to pancreaticoduodenectomy

Author, year published	Types of studies evaluated	Conclusions
Sewnath, 2002	5 RCTs	– No benefit of PBD
	18 RS	– Increased complications due to PBD
		– PBD not recommended routinely
Saleh, 2002	2 RCTs	– No evidence that PBD has positive or negative effect on surgical outcome
	8 RS	
Velanovich, 2009	1 RCT	– PBD increased wound infections by 5 %. Otherwise, no impact
	15 RS	
Garcea, 2010	6 RCTs	– PBD caused bacterial contamination of bile and increased risk of wound infections
	30 RS	
Qiu, 2011	0 RCT	– PBD had no effect on overall morbidity or mortality
	14 RS	
Fang, 2012	6 RCT	– PBD increased risk of morbidity with no effect on mortality
	0 RS	– Evidence does not support or refute routine PBD
Sunm 2014	3 RCTs	– PBD not associated with increased overall morbidity or mortality
	11 RS	– PBD duration <4 weeks increases morbidity
		– Use of PBD selectively (>4 weeks drainage duration and use SEMS rather than plastic stents)

PBD preoperative biliary drainage, *RCTs* randomized controlled trials, *SEMS* self-expandable metal stents

reviewed 14 studies (3 RCTs, 11 RS) comparing PBD using endoscopic stents (plastic or metal) vs. no drainage [98]. The study found no difference in overall mortality or morbidity between the PBD group and the nondrainage group. Interestingly, a subset of the drainage group which had PBD for <4 weeks had an increased overall morbidity by 7–23 %; however, morbidity with PBD for >4 weeks was not significantly different. The authors concluded that PBD should be used selectively, drainage times should be >4 weeks, and SEMS should be used rather than plastic stents. Overall, the published meta-analyses have not definitively demonstrated benefits of PBD on the surgical outcomes of patients with malignant jaundice undergoing pancreaticoduodenectomy. It is important to note that the studies evaluated in various meta-analyses had significant variability in methodology, including older studies, making the data difficult to interpret in light of recent improvements in endoscopic and surgical techniques [11, 99].

The question of whether jaundiced patients with resectable pancreatic head cancer should undergo PBD or proceed directly to surgery was addressed by a recent large multicenter RCT involving community and academic hospitals [100]. Patients with obstructive jaundice and serum bilirubin levels ranging from 2.3 to 14.6 mg/dL were randomized to undergo either endoscopic placement of a plastic biliary stent followed by surgery 4–6 weeks later, or surgery alone within 1 week after diagnosis. The primary outcome was the rate of serious complications within 120 days after randomization. The reported rates of serious complications was 39 % in the early-surgery group vs. 74 % in the PBD group ($p<0.001$). Although PBD was technically successful in 94 % after one or more attempts, the reported failure rate during the initial ERCP was 25 %. Of note, 46 % of patients in the PBD group experienced procedure-related complications such as pancreatitis (7 %), cholangitis (26 %), perforation (2 %), and bleeding (2 %). Surgery-related complications (e.g., infections, bleeding, anastomotic leaks) occurred in 37 % in the early surgery group and 47 % in the PBD group ($p=0.14$). Mortality and length of hospital stay did not differ between the two groups. These results show that patients undergoing PBD have a higher overall complication rate, mainly as a consequence of the PBD procedure itself, and suggest that routine PBD should not be performed. As noted by Baron and Kozarek, the initial ERCP failure rate (25 %) and the procedural complication rate (46 %) reported in this RCT was much higher than reported in most studies for these outcomes (typically 5–10 % for both) [101]. The unexpectedly high rate of cholangitis (26 %) and need for stent exchanges (30 %) in the PBD group during the 4–6 weeks prior to planned surgery can likely be attributed to the use of plastic stents rather than SEMS in this study. As noted previously, multiple studies have shown that SEMS have a superior patency compared to plastic stents and can be used safely in patients who eventually undergo pancreaticoduodenectomy.

Summary and Conclusions

Although EUS with FNA is more sensitive than ERCP for tissue diagnosis of pancreatic cancer, many patients with obstructive jaundice continue to undergo ERCP as the initial procedure. A focal stricture seen in the bile duct and/or pancreatic duct during ERCP in a jaundiced patient should raise suspicion for malignancy and is an opportunity for tissue sampling via brush cytology, forceps biopsy, or both. Using a combination of sampling methods increases sensitivity.

The primary rationale of PBD is to reverse the adverse consequences of biliary obstruction on various organ systems (e.g., immune function, coagulation, renal, cardiovascular) with a goal of reducing complications after major hepatobiliary surgery. However, most clinical trials and numerous meta-analyses have not shown a clear benefit of PBD as a routine procedure for patients with resectable pancreatic cancer who are otherwise able to proceed directly to surgery. The most recent RCT found an alarming rate of PBD-related complications, suggesting that PBD should not be performed routinely [100].

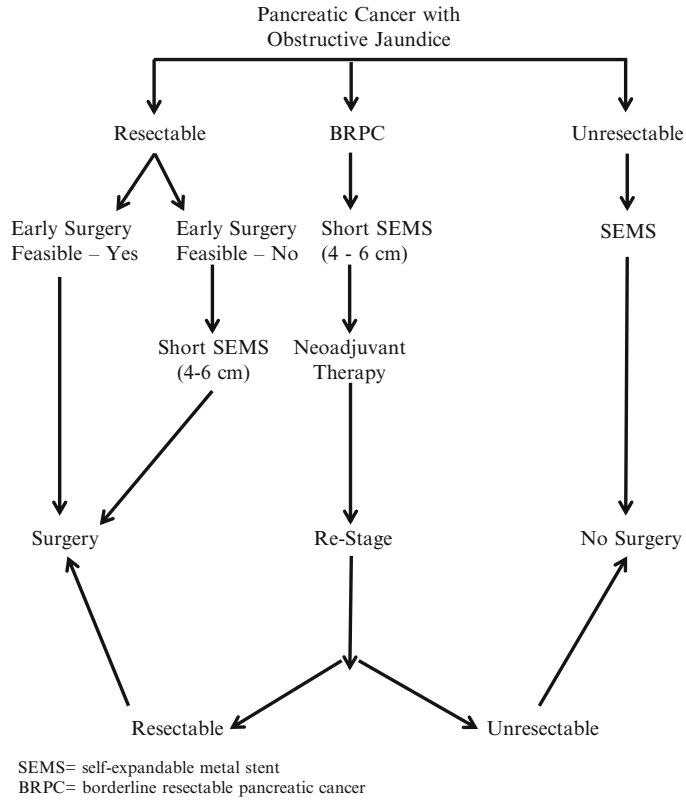

Fig. 4.11 Proposed algorithm for management of patients with obstructive jaundice due to pancreatic cancer

Improved technique and referral of patients to specialized centers with greater expertise could potentially lower the intrinsic risks of PBD.

Despite the controversy regarding its use, selected patients with obstructive jaundice due to resectable or borderline resectable pancreatic could still potentially benefit from PBD (Fig. 4.11). Although acute cholangitis is unusual in malignant obstructive jaundice in the absence of prior biliary intervention, patients who present with cholangitis should undergo urgent biliary decompression [43, 102]. Patients who have surgery delayed due to logistical reasons and those who require medical optimization or further staging should be considered for PBD. Finally, patients who undergo neoadjuvant chemoradiation therapy for borderline resectable pancreatic cancer or as part of treatment protocols may be candidates for PBD as a temporizing measure. In such cases, ERCP with insertion of a short SEMS is the preferred modality. Percutaneous biliary drainage procedures should be reserved for situations when endoscopic stent placement is unsuccessful. EUS-BD is also a feasible salvage technique for unsuccessful ERCP but is currently limited to centers with expertise in therapeutic endoscopy. Multidisciplinary treatment planning should be utilized whenever possible.

References

1. Siegel RL, Miller KD, Jemal A. Cancer statistics, 2015. CA Cancer J Clin. 2015;65(1):5–29.
2. American Cancer Society. What are the key statistics about pancreatic cancer? [updated 01/09/2015; cited 2015 4 April]. http://www.cancer.org/cancer/pancreaticcancer/detailedguide/pancreatic-cancer-key-statistics.
3. Kalser MH, Barkin J, MacIntyre JM. Pancreatic cancer. Assessment of prognosis by clinical presentation. Cancer. 1985;56(2):397–402.
4. Stapley S, Peters TJ, Neal RD, Rose PW, Walter FM, Hamilton W. The risk of pancreatic cancer in symptomatic patients in primary care: a large case-control study using electronic records. Br J Cancer. 2012;106(12):1940–4.

5. Chen VK, Arguedas MR, Baron TH. Expandable metal biliary stents before pancreaticoduodenectomy for pancreatic cancer: a Monte-Carlo decision analysis. Clin Gastroenterol Hepatol. 2005;3(12):1229–37.
6. Artifon EL, Sakai P, Cunha JE, Dupont A, Filho FM, Hondo FY, et al. Surgery or endoscopy for palliation of biliary obstruction due to metastatic pancreatic cancer. Am J Gastroenterol. 2006;101(9):2031–7.
7. Moss AC, Morris E, Leyden J, MacMathuna P. Malignant distal biliary obstruction: a systematic review and meta-analysis of endoscopic and surgical bypass results. Cancer Treat Rev. 2007;33(2):213–21.
8. Adamsen S, Olsen M, Jendresen MB, Holck S, Glenthoj A. Endobiliary brush biopsy: intra- and interobserver variation in cytological evaluation of brushings from bile duct strictures. Scand J Gastroenterol. 2006;41(5):597–603.
9. Adler DG, Baron TH, Davila RE, Egan J, Hirota WK, Leighton JA, et al. ASGE guideline: the role of ERCP in diseases of the biliary tract and the pancreas. Gastrointest Endosc. 2005;62(1):1–8.
10. Hawes RH. Diagnostic and therapeutic uses of ERCP in pancreatic and biliary tract malignancies. Gastrointest Endosc. 2002;56(6 Suppl):S201–5.
11. Singh H, Siddiqui AA. Endosonographic workup and preoperative biliary drainage for pancreatic cancer. Semin Oncol. 2015;42(1):59–69.
12. Jailwala J, Fogel EL, Sherman S, Gottlieb K, Flueckiger J, Bucksot LG, et al. Triple-tissue sampling at ERCP in malignant biliary obstruction. Gastrointest Endosc. 2000;51(4 Pt 1):383–90.
13. Navaneethan U, Njei B, Lourdusamy V, Konjeti R, Vargo JJ, Parsi MA. Comparative effectiveness of biliary brush cytology and intraductal biopsy for detection of malignant biliary strictures: a systematic review and meta-analysis. Gastrointest Endosc. 2015;81(1):168–76.
14. Baron TH, Harewood GC, Rumalla A, Pochron NL, Stadheim LM, Gores GJ, et al. A prospective comparison of digital image analysis and routine cytology for the identification of malignancy in biliary tract strictures. Clin Gastroenterol Hepatol. 2004;2(3):214–9.
15. Zhou GX, Huang JF, Li ZS, Xu GM, Liu F, Zhang H. Detection of K-ras point mutation and telomerase activity during endoscopic retrograde cholangiopancreatography in diagnosis of pancreatic cancer. World J Gastroenterol. 2004;10(9):1337–40.
16. Navaneethan U, Parsi MA, Gutierrez NG, Bhatt A, Venkatesh PG, Lourdusamy D, et al. Volatile organic compounds in bile can diagnose malignant biliary strictures in the setting of pancreatic cancer: a preliminary observation. Gastrointest Endosc. 2014;80(6):1038–45.
17. Deaver JB. The surgery of jaundice. Ann Surg. 1925;81(1):287–98.
18. Whipple AO, Parsons WB, Mullins CR. Treatment of carcinoma of the ampulla of Vater. Ann Surg. 1935;102(4):763–79.
19. Diamond T, Rowlands BJ. Endotoxemia in obstructive jaundice. HPB Surg. 1991;4(2):81–94.
20. Parks RW, Clements WD, Smye MG, Pope C, Rowlands BJ, Diamond T. Intestinal barrier dysfunction in clinical and experimental obstructive jaundice and its reversal by internal biliary drainage. Br J Surg. 1996;83(10):1345–9.
21. Bemelmans MH, Gouma DJ, Greve JW, Buurman WA. Cytokines tumor necrosis factor and interleukin-6 in experimental biliary obstruction in mice. Hepatology. 1992;15(6):1132–6.
22. Kennedy JA, Clements WD, Kirk SJ, McCaigue MD, Campbell GR, Erwin PJ, et al. Characterization of the Kupffer cell response to exogenous endotoxin in a rodent model of obstructive jaundice. Br J Surg. 1999;86(5):628–33.
23. Nehez L, Andersson R. Compromise of immune function in obstructive jaundice. Eur J Surg. 2002;168(6):315–28.
24. Kimmings AN, van Deventer SJ, Obertop H, Rauws EA, Huibregtse K, Gouma DJ. Endotoxin, cytokines, and endotoxin binding proteins in obstructive jaundice and after preoperative biliary drainage. Gut. 2000;46(5):725–31.
25. Pain JA. Reticulo-endothelial function in obstructive jaundice. Br J Surg. 1987;74(12):1091–4.
26. Sokol RJ, Winklhofer-Roob BM, Devereaux MW, McKim Jr JM. Generation of hydroperoxides in isolated rat hepatocytes and hepatic mitochondria exposed to hydrophobic bile acids. Gastroenterology. 1995;109(4):1249–56.
27. Kloek JJ, Heger M, van der Gaag NA, Beuers U, van Gulik TM, Gouma DJ, et al. Effect of preoperative biliary drainage on coagulation and fibrinolysis in severe obstructive cholestasis. J Clin Gastroenterol. 2010;44(9):646–52.
28. Green J, Better OS. Systemic hypotension and renal failure in obstructive jaundice-mechanistic and therapeutic aspects. J Am Soc Nephrol. 1995;5(11):1853–71.
29. Padillo FJ, Cruz A, Briceno J, Martin-Malo A, Pera-Madrazo C, Sitges-Serra A. Multivariate analysis of factors associated with renal dysfunction in patients with obstructive jaundice. Br J Surg. 2005;92(11):1388–92.
30. Padillo J, Puente J, Gomez M, Dios F, Naranjo A, Vallejo JA, et al. Improved cardiac function in patients with obstructive jaundice after internal biliary drainage: hemodynamic and hormonal assessment. Ann Surg. 2001;234(5):652–6.
31. Speer AG, Cotton PB, Russell RC, Mason RR, Hatfield AR, Leung JW, et al. Randomised trial of endoscopic versus percutaneous stent insertion in malignant obstructive jaundice. Lancet. 1987;2(8550):57–62.

32. Catalano D, Mariosa L, Miracco A, Mauro R. Percutaneous cholangiography with biliary catheterization and drainage. Rass Int Clin Ter. 1961;41:255–67.
33. Glenn F, Evans JA, Mujahed Z, Thorbjarnarson B. Percutaneous transhepatic cholangiography. Ann Surg. 1962;156:451–62.
34. Covey AM, Brown KT. Percutaneous transhepatic biliary drainage. Tech Vasc Interv Radiol. 2008;11(1):14–20.
35. Briggs CD, Irving GR, Cresswell A, Peck R, Lee F, Peterson M, et al. Percutaneous transhepatic insertion of self-expanding short metal stents for biliary obstruction before resection of pancreatic or duodenal malignancy proves to be safe and effective. Surg Endosc. 2010;24(3):567–71.
36. Lawson AJ, Beningfield SJ, Krige JE, Rischbieter P, Burmeister S. Percutaneous transhepatic self-expanding metal stents for palliation of malignant biliary obstruction. S Afr J Surg. 2012;50(3):54, 56, 58 passim.
37. Mahgerefteh S, Hubert A, Klimov A, Bloom AI. Clinical impact of percutaneous transhepatic insertion of metal biliary endoprostheses for palliation of jaundice and facilitation of chemotherapy. Am J Clin Oncol. 2013.
38. Pinol V, Castells A, Bordas JM, Real MI, Llach J, Montana X, et al. Percutaneous self-expanding metal stents versus endoscopic polyethylene endoprostheses for treating malignant biliary obstruction: randomized clinical trial. Radiology. 2002;225(1):27–34.
39. Prachayakul V, Aswakul P. Endoscopic ultrasound-guided biliary drainage as an alternative to percutaneous drainage and surgical bypass. World J Gastrointest Endosc. 2015;7(1):37–44.
40. Boulay BR, Parepally M. Managing malignant biliary obstruction in pancreas cancer: choosing the appropriate strategy. World J Gastroenterol. 2014;20(28):9345–53.
41. Robson PC, Heffernan N, Gonen M, Thornton R, Brody LA, Holmes R, et al. Prospective study of outcomes after percutaneous biliary drainage for malignant biliary obstruction. Ann Surg Oncol. 2010;17(9):2303–11.
42. Neal CP, Thomasset SC, Bools D, Sutton CD, Garcea G, Mann CD, et al. Combined percutaneous-endoscopic stenting of malignant biliary obstruction: results from 106 consecutive procedures and identification of factors associated with adverse outcome. Surg Endosc. 2010;24(2):423–31.
43. Bonin EA, Baron TH. Preoperative biliary stents in pancreatic cancer. J Hepatobiliary Pancreat Sci. 2011;18(5):621–9.
44. Moss AC, Morris E, Mac Mathuna P. Palliative biliary stents for obstructing pancreatic carcinoma. Cochrane Database Syst Rev. 2006;(1):Cd004200.
45. Pfau PR, Pleskow DK, Banerjee S, Barth BA, Bhat YM, Desilets DJ, et al. Pancreatic and biliary stents. Gastrointest Endosc. 2013;77(3):319–27.
46. van Berkel AM, van Marle J, Groen AK, Bruno MJ. Mechanisms of biliary stent clogging: confocal laser scanning and scanning electron microscopy. Endoscopy. 2005;37(8):729–34.
47. Saxena P, Kumbhari V, Zein ME, Khashab MA. Preoperative biliary drainage. Dig Endosc. 2015;27(2):265–77.
48. Boulay BR, Gardner TB, Gordon SR. Occlusion rate and complications of plastic biliary stent placement in patients undergoing neoadjuvant chemoradiotherapy for pancreatic cancer with malignant biliary obstruction. J Clin Gastroenterol. 2010;44(6):452–5.
49. England RE, Martin DF, Morris J, Sheridan MB, Frost R, Freeman A, et al. A prospective randomised multicentre trial comparing 10 Fr Teflon Tannenbaum stents with 10 Fr polyethylene Cotton-Leung stents in patients with malignant common duct strictures. Gut. 2000;46(3):395–400.
50. Terruzzi V, Comin U, De Grazia F, Toti GL, Zambelli A, Beretta S, et al. Prospective randomized trial comparing Tannenbaum Teflon and standard polyethylene stents in distal malignant biliary stenosis. Gastrointest Endosc. 2000;51(1):23–7.
51. Kadakia SC, Starnes E. Comparison of 10 French gauge stent with 11.5 French gauge stent in patients with biliary tract diseases. Gastrointest Endosc. 1992;38(4):454–9.
52. Galandi D, Schwarzer G, Bassler D, Allgaier HP. Ursodeoxycholic acid and/or antibiotics for prevention of biliary stent occlusion. Cochrane Database Syst Rev. 2002;(3):Cd003043.
53. Davids PH, Groen AK, Rauws EA, Tytgat GN, Huibregtse K. Randomised trial of self-expanding metal stents versus polyethylene stents for distal malignant biliary obstruction. Lancet. 1992;340(8834–8835):1488–92.
54. Decker C, Christein JD, Phadnis MA, Wilcox CM, Varadarajulu S. Biliary metal stents are superior to plastic stents for preoperative biliary decompression in pancreatic cancer. Surg Endosc. 2011;25(7):2364–7.
55. Kaassis M, Boyer J, Dumas R, Ponchon T, Coumaros D, Delcenserie R, et al. Plastic or metal stents for malignant stricture of the common bile duct? Results of a randomized prospective study. Gastrointest Endosc. 2003;57(2):178–82.
56. Yoon WJ, Ryu JK, Yang KY, Paik WH, Lee JK, Woo SM, et al. A comparison of metal and plastic stents for the relief of jaundice in unresectable malignant biliary obstruction in Korea: an emphasis on cost-effectiveness in a country with a low ERCP cost. Gastrointest Endosc. 2009;70(2):284–9.
57. Adams MA, Anderson MA, Myles JD, Khalatbari S, Scheiman JM. Self-expanding metal stents (SEMS) provide superior outcomes compared to plastic stents for pancreatic cancer patients undergoing neoadjuvant therapy. J Gastrointest Oncol. 2012;3(4):309–13.

58. Wasan SM, Ross WA, Staerkel GA, Lee JH. Use of expandable metallic biliary stents in resectable pancreatic cancer. Am J Gastroenterol. 2005;100(9):2056–61.
59. Boulay BR. Biliary stents for pancreas cancer with obstruction: the problem with plastic. J Gastrointest Oncol. 2012;3(4):306–8.
60. Aadam AA, Evans DB, Khan A, Oh Y, Dua K. Efficacy and safety of self-expandable metal stents for biliary decompression in patients receiving neoadjuvant therapy for pancreatic cancer: a prospective study. Gastrointest Endosc. 2012;76(1):67–75.
61. Kahaleh M, Brock A, Conaway MR, Shami VM, Dumonceau JM, Northup PG, et al. Covered self-expandable metal stents in pancreatic malignancy regardless of resectability: a new concept validated by a decision analysis. Endoscopy. 2007;39(4):319–24.
62. Lawrence C, Howell DA, Conklin DE, Stefan AM, Martin RF. Delayed pancreaticoduodenectomy for cancer patients with prior ERCP-placed, nonfore-shortening, self-expanding metal stents: a positive outcome. Gastrointest Endosc. 2006;63(6):804–7.
63. Siddiqui AA, Mehendiratta V, Loren D, Kowalski T, Fang J, Hilden K, et al. Self-expanding metal stents (SEMS) for preoperative biliary decompression in patients with resectable and borderline-resectable pancreatic cancer: outcomes in 241 patients. Dig Dis Sci. 2013;58(6):1744–50.
64. Mullen JT, Lee JH, Gomez HF, Ross WA, Fukami N, Wolff RA, et al. Pancreaticoduodenectomy after placement of endobiliary metal stents. J Gastrointest Surg. 2005;9(8):1094–104; discussion 104–5.
65. Misra SP, Dwivedi M. Reflux of duodenal contents and cholangitis in patients undergoing self-expanding metal stent placement. Gastrointest Endosc. 2009;70(2):317–21.
66. Parkdo H, Kim MH, Choi JS, Lee SS, Seo DW, Kim JH, et al. Covered versus uncovered wallstent for malignant extrahepatic biliary obstruction: a cohort comparative analysis. Clin Gastroenterol Hepatol. 2006;4(6):790–6.
67. Yoon WJ, Lee JK, Lee KH, Lee WJ, Ryu JK, Kim YT, et al. A comparison of covered and uncovered Wallstents for the management of distal malignant biliary obstruction. Gastrointest Endosc. 2006;63(7):996–1000.
68. Loew BJ, Howell DA, Sanders MK, Desilets DJ, Kortan PP, May GR, et al. Comparative performance of uncoated, self-expanding metal biliary stents of different designs in 2 diameters: final results of an international multicenter, randomized, controlled trial. Gastrointest Endosc. 2009;70(3):445–53.
69. Yang KY, Ryu JK, Seo JK, Woo SM, Park JK, Kim YT, et al. A comparison of the Niti-D biliary uncovered stent and the uncovered Wallstent in malignant biliary obstruction. Gastrointest Endosc. 2009;70(1):45–51.
70. Kullman E, Frozanpor F, Soderlund C, Linder S, Sandstrom P, Lindhoff-Larsson A, et al. Covered versus uncovered self-expandable nitinol stents in the palliative treatment of malignant distal biliary obstruction: results from a randomized, multicenter study. Gastrointest Endosc. 2010;72(5):915–23.
71. Telford JJ, Carr-Locke DL, Baron TH, Poneros JM, Bounds BC, Kelsey PB, et al. A randomized trial comparing uncovered and partially covered self-expandable metal stents in the palliation of distal malignant biliary obstruction. Gastrointest Endosc. 2010;72(5):907–14.
72. Isayama H, Komatsu Y, Tsujino T, Sasahira N, Hirano K, Toda N, et al. A prospective randomised study of "covered" versus "uncovered" diamond stents for the management of distal malignant biliary obstruction. Gut. 2004;53(5):729–34.
73. Saleem A, Leggett CL, Murad MH, Baron TH. Meta-analysis of randomized trials comparing the patency of covered and uncovered self-expandable metal stents for palliation of distal malignant bile duct obstruction. Gastrointest Endosc. 2011;74(2):321–7. e1–3.
74. Almadi MA, Barkun AN, Martel M. No benefit of covered vs. uncovered self-expandable metal stents in patients with malignant distal biliary obstruction: a meta-analysis. Clin Gastroenterol Hepatol. 2013;11(1):27–37.e1.
75. Fumex F, Coumaros D, Napoleon B, Barthet M, Laugier R, Yzet T, et al. Similar performance but higher cholecystitis rate with covered biliary stents: results from a prospective multicenter evaluation. Endoscopy. 2006;38(8):787–92.
76. Suk KT, Kim HS, Kim JW, Baik SK, Kwon SO, Kim HG, et al. Risk factors for cholecystitis after metal stent placement in malignant biliary obstruction. Gastrointest Endosc. 2006;64(4):522–9.
77. Artifon EL, Sakai P, Ishioka S, Marques SB, Lino AS, Cunha JE, et al. Endoscopic sphincterotomy before deployment of covered metal stent is associated with greater complication rate: a prospective randomized control trial. J Clin Gastroenterol. 2008;42(7):815–9.
78. Banerjee N, Hilden K, Baron TH, Adler DG. Endoscopic biliary sphincterotomy is not required for transpapillary SEMS placement for biliary obstruction. Dig Dis Sci. 2011;56(2): 591–5.
79. Giovannini M, Moutardier V, Pesenti C, Bories E, Lelong B, Delpero JR. Endoscopic ultrasound-guided bilioduodenal anastomosis: a new technique for biliary drainage. Endoscopy. 2001;33(10): 898–900.
80. Artifon EL, Aparicio D, Paione JB, Lo SK, Bordini A, Rabello C, et al. Biliary drainage in patients with unresectable, malignant obstruction where ERCP fails: endoscopic ultrasonography-guided choledo-choduodenostomy versus percutaneous drainage. J Clin Gastroenterol. 2012;46(9):768–74.

81. Dhir V, Artifon EL, Gupta K, Vila JJ, Maselli R, Frazao M, et al. Multicenter study on endoscopic ultrasound-guided expandable biliary metal stent placement: choice of access route, direction of stent insertion, and drainage route. Dig Endosc. 2014;26(3):430–5.
82. Gupta K, Perez-Miranda M, Kahaleh M, Artifon EL, Itoi T, Freeman ML, et al. Endoscopic ultrasound-assisted bile duct access and drainage: multicenter, long-term analysis of approach, outcomes, and complications of a technique in evolution. J Clin Gastroenterol. 2014;48(1):80–7.
83. Iwashita T, Doi S, Yasuda I. Endoscopic ultrasound-guided biliary drainage: a review. Clin J Gastroenterol. 2014;7:94–102.
84. Kawakubo K, Isayama H, Kato H, Itoi T, Kawakami H, Hanada K, et al. Multicenter retrospective study of endoscopic ultrasound-guided biliary drainage for malignant biliary obstruction in Japan. J Hepatobiliary Pancreat Sci. 2014;21(5):328–34.
85. Khashab MA, Valeshabad AK, Modayil R, Widmer J, Saxena P, Idrees M, et al. EUS-guided biliary drainage by using a standardized approach for malignant biliary obstruction: rendezvous versus direct transluminal techniques (with videos). Gastrointest Endosc. 2013;78(5):734–41.
86. Song TJ, Hyun YS, Lee SS, Park DH, Seo DW, Lee SK, et al. Endoscopic ultrasound-guided choledochoduodenostomies with fully covered self-expandable metallic stents. World J Gastroenterol. 2012;18(32):4435–40.
87. Vila JJ, Perez-Miranda M, Vazquez-Sequeiros E, Abadia MA, Perez-Millan A, Gonzalez-Huix F, et al. Initial experience with EUS-guided cholangiopancreatography for biliary and pancreatic duct drainage: a Spanish national survey. Gastrointest Endosc. 2012;76(6):1133–41.
88. Shah JN, Marson F, Weilert F, Bhat YM, Nguyen-Tang T, Shaw RE, et al. Single-operator, single-session EUS-guided anterograde cholangiopan-creatography in failed ERCP or inaccessible papilla. Gastrointest Endosc. 2012;75(1):56–64.
89. Jinkins LJ, Parmar AD, Han Y, Duncan CB, Sheffield KM, Brown KM, et al. Current trends in preoperative biliary stenting in patients with pancreatic cancer. Surgery. 2013;154(2):179–89.
90. Sargent M, Boeck S, Heinemann V, Jauch KW, Seufferlein T, Bruns CJ. Surgical treatment concepts for patients with pancreatic cancer in Germany—results from a national survey conducted among members of the "Chirurgische Arbeitsgemeinschaft Onkologie" (CAO) and the "Arbeitsgemeinschaft Internistische Onkologie" (AIO) of the Germany Cancer Society (DKG). Langenbecks Arch Surg. 2011;396(2):223–9.
91. Garcea G, Chee W, Ong SL, Maddern GJ. Preoperative biliary drainage for distal obstruction: the case against revisited. Pancreas. 2010;39(2):119–26.
92. Qiu YD, Bai JL, Xu FG, Ding YT. Effect of preoperative biliary drainage on malignant obstructive jaundice: a meta-analysis. W J Gastroenterol. 2011;17(3):391–6.
93. Saleh MM, Norregaard P, Jorgensen HL, Andersen PK, Matzen P. Preoperative endoscopic stent placement before pancreaticoduodenectomy: a meta-analysis of the effect on morbidity and mortality. Gastrointest Endosc. 2002;56(4):529–34.
94. Sewnath ME, Karsten TM, Prins MH, Rauws EJ, Obertop H, Gouma DJ. A meta-analysis on the efficacy of preoperative biliary drainage for tumors causing obstructive jaundice. Ann Surg. 2002;236(1):17–27.
95. Velanovich V, Kheibek T, Khan M. Relationship of postoperative complications from preoperative biliary stents after pancreaticoduodenectomy. A new cohort analysis and meta-analysis of modern studies. JOP. 2009;10(1):24–9.
96. Wang Q, Gurusamy KS, Lin H, Xie X, Wang C. Preoperative biliary drainage for obstructive jaundice. Cochrane Database Syst Rev. 2008(3):Cd005444.
97. Fang Y, Gurusamy KS, Wang Q, Davidson BR, Lin H, Xie X, et al. Pre-operative biliary drainage for obstructive jaundice. Cochrane Database Syst Rev. 2012;(9):Cd005444.
98. Sun C, Yan G, Li Z, Tzeng CM. A meta-analysis of the effect of preoperative biliary stenting on patients with obstructive jaundice. Medicine. 2014;93(26), e189.
99. de Bellis M, Palaia R, Sandomenico C, Di Girolamo E, Cascella M, Fiore F. Is preoperative endoscopic biliary drainage indicated for jaundiced patients with resectable pancreatic cancer? Curr Drug Targets. 2012;13(6):753–63.
100. van der Gaag NA, Rauws EA, van Eijck CH, Bruno MJ, van der Harst E, Kubben FJ, et al. Preoperative biliary drainage for cancer of the head of the pancreas. N Engl J Med. 2010;362(2):129–37.
101. Baron TH, Kozarek RA. Preoperative biliary stents in pancreatic cancer—proceed with caution. N Engl J Med. 2010;362(2):170–2.
102. Rerknimitr R, Kullavanijaya P. Operable malignant jaundice: to stent or not to stent before the operation? World J Gastrointest Endosc. 2010;2(1):10–4.