Role of Endoscopic Ultrasonography and Endoscopic Retrograde Cholangiopancreatography in the Clinical Assessment of Pancreatic Neoplasms

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KEYWORDS
- Endoscopic ultrasonography
- Fine-needle aspiration
- Endoscopic retrograde cholangiopancreatography
- Pancreatic cancer
- Pancreatic cyst neoplasm
- Biliary decompression

KEY POINTS
- Endoscopic ultrasonography (EUS)–guided fine-needle aspiration is an accurate technique for establishing tissue diagnosis in patients with pancreatic mass lesions.
- There has been growing interest in evaluating core tissue specimens procured by EUS for molecular markers that may serve as prognostic predictors and targets for focused therapy in pancreatic cancer.
- Endoscopic retrograde cholangiopancreatography (ERCP) with biliary stent placement relieves obstructive jaundice and is widely practiced both as a palliative measure and for preoperative biliary decompression in pancreatic cancer.
- EUS-guided drainage is becoming an effective rescue therapy for relief of obstructive jaundice in patients who fail ERCP, and it may be superior to percutaneous transhepatic biliary drainage.

ENDOSCOPIC ULTRASONOGRAPHY IN PANCREATIC NEOPLASMS

Endoscopic ultrasonography (EUS) is a sensitive technology for detecting pancreatic lesions and for performing fine-needle aspiration (FNA). Although computed tomography (CT) and magnetic resonance cholangiopancreatography are excellent modalities...
for imaging the pancreas, neuroendocrine tumors and pancreatic cyst lesions are better characterized by EUS. The diagnostic sensitivity of EUS-guided FNA (EUS-FNA) exceeds 85% to 90% and it is significantly superior to percutaneous techniques. In addition, EUS enables additional interventions, such as celiac plexus neurolysis (CPN) for palliation of pain, fiducial placements to facilitate intraoperative identification of small tumors or improved targeting of image-guided radiation therapy, and drainage of well-encapsulated pancreatic fluid collections after a distal pancreatectomy. The diagnostic and therapeutic applications of EUS in pancreatic neoplasms are discussed here.

Pancreatic Cancer

**Staging endoscopic ultrasonography**

Staging of pancreatic malignancy is performed according to the American Joint Committee for Cancer Staging TNM (tumor, node, metastasis) classification. Reported accuracies of EUS range from 63% to 94% for T classification and 41% to 86% for N classification. Although early studies found that EUS was superior to conventional CT for T and N staging, recent studies report that EUS is not superior to CT and MRI for T and N staging of pancreatic tumors. The initial advantages shown by EUS compared with the other imaging modalities for staging of pancreatic tumors were not confirmed in subsequent studies.

The sensitivity and specificity of EUS for malignant vascular invasion are 42% to 91% and 89% to 100%, respectively. Although some studies show that EUS is more accurate than CT for vascular invasion, other investigators have reported that the accuracy of CT is superior to that of EUS. The overall accuracy of MRI is reportedly equivalent or superior to that of EUS. The overall sensitivity and accuracy of EUS for arterial invasion are 56% and 50%, respectively. The sensitivity of EUS for tumor invasion of the portal vein or portal vein confluence is 60% to 100%, with most studies showing sensitivities of more than 80% (Fig. 1). The sensitivity of EUS for portal vein invasion is also consistently superior to that of CT. For the superior mesenteric vein (SMV), superior mesenteric artery (SMA), and celiac artery, the sensitivity of EUS is only 17% to 83%, 17%, and 50%, respectively. The sensitivity and specificity of EUS for determining resectability of pancreatic cancer in a pooled analysis of 377 patients was 69% (range, 23%–91%) and 82% (63%–100%), respectively. The overall EUS accuracy for tumor resectability was reported at 77%. Thus, more cost and decision analysis and comparative

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**Fig. 1.** EUS reveals a 2-cm hypoechoic pancreatic head mass (arrow) invading the confluence of the portal vein. PV, portal vein; SMV, superior mesenteric vein; SPL, splenic vein; VN, vein.
Endoscopic ultrasonography fine-needle aspiration

Two recently published meta-analyses totaling more than 8400 patients and 67 studies reported pooled sensitivities for the diagnosis of malignancy based on cytology of 85% and 89% and pooled specificities of 98% and 99%. However, the negative predictive value of EUS-FNA for pancreatic tumors remains limited at 65%. Therefore a negative or nondiagnostic biopsy does not exclude the possibility of malignancy. Fritscher-Ravens and colleagues found that, in a series of 207 consecutive patients with focal pancreatic lesions, the sensitivity of EUS-FNA for the diagnosis of malignancy in patients with normal parenchyma (89%) was superior to the sensitivity in those with chronic pancreatitis (54%). The presence of chronic pancreatitis may also hinder cytologic interpretation of pancreatic biopsy, thus decreasing the sensitivity of EUS-FNA of pancreatic masses. In a meta-analysis of 34 studies that evaluated the diagnostic accuracy of EUS-FNA for pancreatic cancer in 3644 patients with solid pancreatic mass lesions, rapid on-site evaluation (ROSE) was a significant determinant of EUS-FNA accuracy. Also, at least 5 to 7 EUS-FNA passes should be performed when sampling pancreatic masses to maximize diagnostic yield (Fig. 2) and this information may prove helpful to endosonographers performing EUS-FNA when ROSE is not available.

Occasionally, ROSE may be inconclusive because of tumor necrosis, fibrosis, or hypervascularity. The diagnostic yield may be increased by fanning the lesion, in which different angles of scope deflection are used in order to sample the peripheral parts of the lesion. In a recent randomized study by these authors, the fanning technique was superior to the standard approach, with fewer passes being required to establish a diagnosis.

The most commonly used commercially available EUS-FNA needle sizes are 19, 22, and 25 gauge. In a recent meta-analysis of 8 studies comprising 1292 patients, 25-gauge needles were associated with higher sensitivity but comparable specificity with 22-gauge needles. In general, 25-gauge needles are associated with lower technical failures compared with 19-gauge and 22-gauge needles when sampling pancreatic head and uncinate process lesions.

Postprocedure adverse events following EUS-FNA are rare. In a recent systematic review that included 8246 patients with pancreatic lesions, 7337 of those being solid masses, minor adverse events after EUS-FNA occurred in 60 patients (0.82%), which included pancreatitis, abdominal pain, bleeding, fever, and infection.

Fig. 2. (A) EUS-FNA of a 3-cm pancreatic head mass. (B) Rapid on-site evaluation reveals atypical ductal cells consistent with pancreatic adenocarcinoma. (Diff-Quik, original magnification ×100)
Pancreatic Neuroendocrine Tumors

Pancreatic neuroendocrine tumors (PNETs) represent less than 10% of pancreatic tumors. In a series of studies that compared EUS with other imaging modalities, the sensitivity of EUS for detection of PNETs was 77% to 94%.\textsuperscript{24,25} EUS seems especially useful for detection of small PNETs (<2.5 cm) missed by other imaging studies. In a study of 30 patients with 32 insulinomas, the sensitivity of EUS was 94% compared with 29% for nonhelical CT and 57% for dual-phase multidetector CT.\textsuperscript{24} In another study of 217 patients,\textsuperscript{25} CT was more likely than EUS to miss insulinomas and PNETs less than 2 cm. These investigators also found that the overall sensitivity of EUS (91%) was greater than that of CT (63%). In recent studies, the reported sensitivity of MRI for PNET detection is 85% to 100%\textsuperscript{26,27} with positive predictive value of 96%.\textsuperscript{28}

In a series of patients with histologically proven insulinomas (n = 20) or gastrinomas (n = 21), the sensitivity and positive predictive value of EUS were 77% and 94%, respectively.\textsuperscript{29} For the same patients, the sensitivity and positive predictive value of somatostatin receptor scintigraphy (SRS) for insulinoma and gastrinoma detection were 60% and 100%, and 25% and 100%, respectively. When both tests were combined and a subgroup analysis was performed, the overall sensitivity of combined EUS and SRS was 89% for insulinomas and 93% for gastrinomas. It seems that the combination of EUS and SRS may optimize preoperative identification of PNETs and limit the need for more invasive tests such as angiography. As with pancreatic cancer, EUS-FNA seems to be an excellent modality for establishing tissue diagnosis in PNETs (Fig. 3). In a recent meta-analysis of 13 studies comprising 456 patients, the pooled sensitivity of EUS for detecting PNET was 87% and the pooled specificity was 98%.\textsuperscript{30}

Pancreatic Cyst Lesions

When a cystic lesion has been identified in the pancreas, the size, location, relation to adjacent vessels and organs, and the presence of locoregional or distant metastases should be noted. The cyst should be examined to determine the wall thickness, presence of a mural nodule, or associated mass. The size of the main pancreatic duct, whether it communicates with the cyst, the presence of mucin or a mural nodule within the pancreatic duct, or any focal dilatation should also be noted.

There are several features on EUS that are worrisome for malignant transformation of the cyst and these include thick wall or septum, an associated solid mass, or a mural nodule (Fig. 4). The presence of focal dilatation of the main pancreatic duct, pancreatic duct measuring greater than or equal to 10 mm, or mural nodules are features associated with malignant transformation (See Greer JB, Ferrone CR: Spectrum and classification of cystic neoplasms of the pancreas, in this issue).

Fig. 3. (A) EUS-FNA of a well-circumscribed 1.2-cm hypoechoic mass in the pancreatic tail region. (B) Rapid on-site evaluation of the pancreatic tail mass is suggestive of a neuroendocrine tumor. (Diff-Quik, original magnification ×200)
The risk of adverse events from EUS-FNA of pancreatic cysts is slightly higher than that resulting from EUS-FNA of a solid lesion. In a recent review of adverse events associated with EUS-FNA, the most common adverse event was pancreatitis, which occurred in 1.1% of patients, followed by pain (0.77%), bleeding (0.33%), fever (0.33%), and infection (0.22%). Antibiotic prophylaxis is therefore recommended, usually with intravenous ciprofloxacin before the procedure. If FNA is performed, the aspirate must be sent for carcinoembryonic antigen (CEA) and/or cytology.

The specificity of cytology for malignancy is excellent and approaches 100%, but the sensitivity varies considerably in reported series. This finding reflects the difficulty in interpreting these lesions, especially when the cellularity of the samples is low. Brandwein and colleagues and Brugge and colleagues reported sensitivities of 55% and 59%, respectively, for differentiating benign from malignant or potentially malignant pancreatic cysts. The CEA levels are higher in mucinous than in nonmucinous cysts, with a reference value of 192 ng/mL for mucinous cysts. In a large study, the diagnostic accuracy of this reference level for differentiating mucinous from non-mucinous cysts was 79%. Although molecular markers such as KRAS and GNAS are being studied as indicators of malignant transformation, data are limited and further research is needed before they can be incorporated into clinical practice.

**The Concept of Core Biopsy**

Although considerable progress has been made in the treatment of breast and lung cancers in which the delivery of chemotherapy is guided by the expression of molecular markers in the tumor, which can in turn help prognosticate the tumor and guide treatment algorithms, data on personalized therapy in pancreatic cancer are scant. There is growing evidence that immune cells in pancreatic ductal adenocarcinoma produce immune suppressive signals that allow tumors to evade the immune response. Also, the stromal fibroblasts provide a protective environment that not only supports and promotes pancreatic adenocarcinoma tumor growth and progression but also likely suppresses the development of and/or access to the antitumor immune responses. Strategies to deplete the desmoplastic stroma before institution of immune therapy could promote robust response against tumor cells. Therefore, it is increasingly apparent that the evaluation of fibrous stroma for molecular markers may be an integral part of cancer therapy. Preliminary evidence in our laboratory suggests that specimens procured using a 19-gauge or 22-gauge FNA needle and fixed in formalin have preserved microcores that enable detailed assessment of the

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**Fig. 4.** EUS reveals an anechoic cyst in the pancreatic head with thick peripheral rim walls (arrow). EUS-FNA proved the lesion to be a cystic neuroendocrine tumor.
histologic architecture with neoplastic glands embedded in the stroma. Randomized trials are in progress to identify the best technique for core tissue procurement. We believe that the results of these trials will be of significant help in advancing personalized therapy in pancreatic cancer.

**Therapeutic Applications of Endoscopic Ultrasonography in Pancreatic Neoplasms**

**Endoscopic ultrasonography–guided celiac plexus neurolysis**

At EUS, after identifying the celiac artery take-off from the aorta, the FNA needle is positioned adjacent and anterior to the lateral aspect of the aorta at the level of the celiac trunk (Fig. 5). The FNA needle is then aspirated to rule out vessel penetration before injection. For CPN in patients with pancreatic cancer, 10 mL of 0.25% bupivacaine are injected followed by 10 mL of dehydrated (98%) alcohol. A recent meta-analysis reported that 80% of patients with pancreatic cancer undergoing CPN had pain relief.34 Also, patients who had injections on both sides of the celiac artery had a higher rate of pain relief than those who received injections only on 1 side (85% vs 46%). In a randomized trial, 96 patients with inoperable pancreatic cancer were assigned to either CPN or conventional pain management.35 At 3 months, patients treated with CPN had significantly greater pain relief, with a trend toward lower morphine consumption. There was no difference between the two groups in quality-of-life scores or survival.

**Endoscopic ultrasonography–guided implantation therapy**

PNETs are small and tumor localization at laparoscopic surgery can be challenging. EUS-guided fiducial placement is a new technique for intraoperative localization of pancreatic tumors (Fig. 6). At EUS, once a tumor is localized, a small gold fiducial (2–3 mm × 0.8 mm) is back-loaded to a 19-gauge FNA needle (after stylet retraction) and the lumen of the needle is sealed with bone wax. After puncturing the lesion, the stylet is advanced to facilitate deployment of gold fiducials within the tumor. At surgery, using fluoroscopy, the tumor is identified to facilitate laparoscopic resection.36 Likewise, fiducial placement enables better targeting of pancreatic cancers by image-guided radiation therapy.37

**Endoscopic ultrasonography–guided pancreatic cyst ablation**

Ethanol and chemotherapeutic agents such as paclitaxel are used for EUS-guided ablation of pancreatic cyst lesions under EUS guidance. In a systematic review, 38 the pooled proportion of patients with complete cyst resolution was 56.2%
(95% confidence interval [CI], 48.2%–64.1%) and partial cyst resolution was 23.7% (95% CI, 17.2%–30.9%). Postprocedural adverse events included abdominal pain in 6.5% (95% CI, 3.1%–11.0%) and pancreatitis in 3.9% (95% CI, 1.4–7.6).

**Endoscopic ultrasonography–guided drainage of postoperative pancreatic fluid collections**

Development of a postoperative pancreatic fluid collection is a common complication after distal pancreatectomy and is usually managed by percutaneous drainage. Major disadvantages of percutaneous drainage include fistula formation, infection, skin excoriation, and accidental dislodging of the catheter. At EUS, the pancreatic fluid collection can be easily accessed using a 19-gauge needle. After dilating the transmural tract to 6 to 10 mm, multiple internal stents can be deployed for transgastric drainage (Fig. 7). The treatment success rate for this approach exceeds 90% and it yields faster symptom relief and resolution of the pancreatic fluid collection compared with percutaneous drainage or transpapillary stenting.39,40

**ENDOSCOPIC RETROGRADE CHOLANGIOPANCREATOGRAPHY IN PANCREATIC NEOPLASMS**

The main objective of endoscopic retrograde cholangiopancreatography (ERCP) in patients with pancreatic neoplasm is to provide drainage for obstructive jaundice by placement of self-expandable metal or polyethylene stents. Despite the indispensable role of EUS in tissue acquisition, ERCP presents a unique opportunity to establish a diagnosis of malignancy during a drainage procedure, thereby saving the patient subsequent unnecessary and expensive procedures. The outcomes of different techniques adopted at ERCP for tissue sampling are reviewed here, and an objective assessment is provided of the role of various endoprostheses in both preoperative and palliative biliary decompression.
Rationale for Tissue Sampling

Although EUS-FNA is currently the technique of choice for tissue acquisition in pancreatic cancer, most patients with malignant biliary obstruction require ERCP for relief of jaundice. In addition, only 15% of patients presenting with malignant obstructive jaundice undergo an attempt at surgical curative resection. Therefore, it is logical to attempt tissue sampling before biliary stent placement in this patient cohort because it obviates an additional procedure, namely EUS.

The diagnostic yield of tissue sampling is influenced by tumor cellularity and its differentiation. Pancreatic cancer stimulates a desmoplastic and fibrotic reaction making the tumor very dense and low in cellularity. Establishing a definitive diagnosis in these patients therefore requires sampling of layers deeper than the surface epithelium via a biliary biopsy and superficial sampling of the tumor by techniques such as brush cytology often yields an acellular or false-negative specimen. Well-differentiated tumors can also be difficult to diagnose by cytology and large histologic specimens are often necessary to enable pathologists to differentiate cancer from normal tissue. When the clinical suspicion for malignancy remains high, but cytology is inconclusive, it may be necessary to perform a biopsy for histologic confirmation. There is increasing recognition of autoimmune pancreatitis, a condition that can cause obstructive jaundice and mimic pancreatic cancer. This benign disorder responds well

Fig. 7. (A) CT of the abdomen revealing a pancreatic fluid collection after distal pancreatectomy measuring 7 × 6 cm in the lesser sac. (B) The pancreatic fluid collection is accessed using a 19-gauge needle under EUS guidance. (C) Transesophageal stent was deployed for drainage of the fluid collection. (D) Follow-up CT of the abdomen at 8 weeks reveals near-complete resolution of the pancreatic fluid collection.

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to treatment with corticosteroids and hence must be reliably distinguished from pancreatic cancer.

**Endoscopic Techniques**

The 3 most common tissue acquisition techniques adopted at ERCP are fluoroscopy-guided biliary brushing, fluoroscopy-guided biliary biopsy, and cholangioscopy-guided biopsy.

Biliary brushings are performed using an 8-Fr cytology brush that is advanced over a guidewire that bypasses the stricture (Fig. 8). Because most endoscopists negotiate a guidewire through the stricture as the first major step in the therapeutic goal of biliary stent placement, brushings for tissue sampling can be done at the same time without interrupting this sequence. The reported overall sensitivity for biliary brushings ranges from 8% to 57% depending on the length of the brush, type of bristles, duration of brushing, and type of tumor being sampled. In a recent review, the overall sensitivity of biliary brushings in 837 patients was reported to be 42%. In general, the yield of biliary brushings for pancreatic adenocarcinoma is lower than that for cholangiocarcinoma because the interior of a biliary stricture resulting from pancreatic cancer is composed of benign epithelium that is compressed by surrounding neoplastic tissue. Biliary brushes only scrape the superficial layers of the stricture and therefore are low in yield.

The technique of fluoroscopy-guided forceps biopsy involves the insertion of 5-Fr to 10-Fr devices to the lower edge of the stricture (Fig. 9). Under fluoroscopy, multiple biopsies can be obtained from the lower margin of the apparent tumor. The biopsy forceps are available in several designs: straight, angled, freehand, and over-the-wire devices. In a recent review, the overall sensitivity of forceps biopsy in 502 patients was reported to be 56%.

Given the disappointing results of single sampling techniques, endoscopists currently combine multiple techniques during an ERCP procedure to improve the diagnostic yield. In clinical practice, a cytology brushing is first performed, followed by biopsy of the stricture site. In a study by Ponchon and colleagues, biliary brushing

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**Fig. 8.** Cholangiogram reveals brushing of a distal biliary stricture.
had a sensitivity of 43% and forceps biopsy 30%, but when both of these techniques were combined the yield increased to 63%.

Some investigators combine intraductal FNA during an ERCP procedure. In this technique, a 22-gauge intraductal FNA needle is able to sample deeper layers of a lesion than are afforded by a biliary brush or biopsy forceps. In one study at Indiana University, the combination of all 3 of these techniques (brushing, biopsy, and intraductal FNA), resulted in successful diagnosis in 82% of patients during a single ERCP session. When the results were analyzed, each technique contributed to making the diagnosis in at least some of the patients, implying that, in many patients, only 1 of the 3 techniques was positive and the other 2 were negative or equivocal. Despite the results of this study, this method of triple sampling is impractical because it is time consuming, technically difficult, and ancillary to the main goal of placing a biliary endoprosthesis for biliary decompression.

Cholangioscopy-guided biopsy is a novel technique that is gaining increasing acceptance. This technique involves the use of a so-called mother-daughter scope to sample the biliary lesion. While one endoscopist controls the mother duodenoscope, the second endoscopist maneuvers the daughter cholangioscope, which is advanced from within the biopsy channel of the duodenoscope into the bile duct for tissue sampling. The advantage of this technique is that it enables sampling of the biliary stricture under direct visualization. The disadvantage is that it is cumbersome because it involves 2 endoscopists, requires careful coordination, and the equipment is fragile and expensive. A novel single-operator system called SpyGlass is currently available and being increasingly used for tissue acquisition in the bile duct (Fig. 10). This system uses a disposable high-definition probe with an inbuilt camera and separate miniature channels for passage of biopsy forceps and water for irrigation of the bile duct, and advancement of laser probes for fragmentation of stones. The probe has a 4-way deflection capability that enables movement in both up-down and left-right directions. The targeted lesion can be sampled using mini–biopsy forceps and, if cytopathology support is available, an on-site diagnosis can be

![Fig. 9. Biopsy of a distal biliary stricture performed at ERCP.](image-url)
established rapidly. The diagnostic accuracy of the SpyGlass system when evaluating biliary strictures exceeds 75%.47 A simplified algorithm for tissue acquisition is proposed in Fig. 11.

**Biliary Stenting**

Indications for biliary stenting at ERCP include jaundice, fever, and pruritus. Compared with percutaneous and surgical drainage, endoscopic biliary stenting is associated with lower morbidity and mortality.48,49 The procedure has also been shown to improve symptoms such as anorexia and patient quality of life. In a randomized trial of 201 patients with pancreatic head cancer who underwent surgery or preoperative stent placement, the overall rate of adverse events was significantly higher in the endoscopy cohort, mainly owing to stent-related complications.50 Despite these findings, preoperative drainage is indicated when surgical resection is not imminent.

![Fig. 10. (A) The SpyGlass cholangioscope for evaluating the bile duct at ERCP. (Courtesy of Boston Scientific, Marlborough, MA). (B) A malignant lesion is identified at SpyGlass cholangioscopy in the bile duct.](image)

![Fig. 11. A simplified algorithm for tissue acquisition in patients with a biliary stricture.](image)
Types of Biliary Stents

Plastic stents
The most common sizes of plastic stents placed in the bile duct are 7, 8.5, and 10 Fr. Larger diameter stents perform better than smaller stents because of better flow rates and less stasis. Most stents have side holes to facilitate biliary drainage and are designed with either pigtailis or flaps at either end to prevent migration. Different materials have been used for stent construction, including polyethylene, polyurethane, and Teflon. Teflon stents have the lowest friction coefficient and the best potential for preventing stent clogging. The stents also range in length from 4 to 15 cm.

The choice of stent depends on the location and length of the biliary stricture. Whenever feasible, a 10-Fr plastic stent must be placed in lieu of small-caliber stents given their longer patency. Plastic stents are deployed over a guidewire using a push-catheter and a biliary sphincterotomy is not a prerequisite to stent placement. The stent is positioned with the proximal and distal ends bridging the stricture so as to facilitate free flow of bile into the duodenum. Compared with metal stents, plastic endoprostheses have shorter durations of patency and hence require elective stent exchanges (Fig. 12). The usual time to perform a stent exchange is 10 to 12 weeks. However, plastic stents are much cheaper than metal stents.

Self-expanding metal stents
Metal stents differ in the manner in which they are braided, the size of the mesh, composition, length, width, rigidity, and degree of covering. The usual diameter of the stent is 8 to 10 mm and the length varies between 4 and 12 cm. After deployment, some stents can expand and also shorten by up to 30%. Given their large diameter, metal stents remain patent for longer durations than plastic stents. However, that does not eliminate the risk of stent obstruction (Fig. 13), and the average duration of stent patency is between 6 and 9 months. The mechanism of stent dysfunction differs from that seen in plastic stents and includes tumor ingrowth through the stent interstices, overgrowth at both ends, and intimal hyperplasia. To overcome the problem of tumor ingrowth, self-expandable metal stents have been fully or partially covered with a polyurethane or silicone membrane. Although some studies have shown that stent occlusion caused by tumor ingrowth occurs less frequently

Fig. 12. (A) Cholangiogram reveals a distal biliary stricture in a patient with a pancreatic head mass. (B) Successful deployment of a 10-Fr plastic stent in the bile duct for biliary decompression.
with covered than with uncovered metal stents, these data have been disputed by others.\textsuperscript{51,52} Although data on adverse events are scarce, stent migration, cholecystitis, and pancreatitis seem to occur at a higher rate with covered stents.\textsuperscript{51,52} Covered stents should not be used intrahepatically because of occlusion of the hepatic side branches by the covering membrane. In addition, placement of metal stents can be technically challenging and uncovered metal stents cannot be removed after deployment. Furthermore, metal stents are more expensive than plastic stents.

**Choice of Stent Placement**

**Inoperable cancer**

In a recent randomized trial of 219 patients with extrahepatic biliary obstruction from inoperable cancer, the mean functional time for plastic stents was 172 days and for metal stents was 288 days (\(P<.005\)).\textsuperscript{53} Given the longer duration of patency, self-expanding metal stents should ideally be placed in all patients but their high costs have limited their use to specific settings. In a cost-effective approach, the choice of stent depends mainly on an estimate of patient survival. Patients with liver metastases and poor functional status have a short survival time (<3 months) and should preferably be treated with plastic stents. In contrast, patients with longer life expectancy (>3 months; ie, patients with no liver metastasis, good functional status, and/or undergoing chemotherapy) should preferably be treated with metal stents. Also, patients who present with early obstruction of plastic stents (ie, within 1 month) should receive a self-expandable metal stent.

**Preoperative biliary decompression**

Based on the findings of a recent randomized trial in which patients undergoing preoperative ERCP had poor clinical outcomes, biliary stenting should not be performed routinely in all operable patients.\textsuperscript{50} However, in patients with intractable pruritus or cholangitis, biliary stent placement can be performed after interdisciplinary consultation. Also, some surgeons prefer placement of biliary stents in patients with obstructive jaundice before performing a Whipple procedure because of concerns of metabolic derangement. In such instances, we have shown that the placement of a fully covered metal stent 2 cm below the liver hilum
provides symptomatic relief and does not adversely affect clinical or surgical outcomes.\textsuperscript{54}

\textbf{Technical Outcomes}

The technical success rate for biliary stenting at ERCP exceeds 85\% and approaches 95\% to 99\% in expert hands.\textsuperscript{55} Although standard cannulation techniques facilitate biliary access in most patients, advanced techniques, such as pre-cut sphincterotomy, transpapillary pancreatic sphincterotomy, fistulotomy, and cannulation over a pancreatic duct stent, may be required when standard techniques fail. Advanced cannulation techniques confer higher risks and are associated with a 5\% to 10\% rate of adverse events that include pancreatitis, bleeding, perforation, pneumoperitoneum, and abdominal pain.\textsuperscript{56,57} Patients with failed biliary access using standard cannulation techniques preferably should be referred to tertiary centers with advanced expertise for a repeat ERCP procedure. Several studies have shown that the technical success rate for repeat ERCP at expert centers exceeds 90\%.\textsuperscript{55,58}

\textbf{Endoscopic Treatment Alternatives}

Although percutaneous transhepatic biliary drainage and surgical biliary bypass are considered the main treatment alternatives following a failed ERCP, EUS-guided biliary drainage is becoming increasingly popular as a rescue technique. At EUS, the dilated extrahepatic bile duct or intrahepatic duct radicle is identified and punctured using a 19-gauge needle. After the passage of a stiff guidewire, the transmural tract is dilated and a fully covered metal stent is deployed for biliary drainage. The technical success rate for EUS-guided biliary drainage exceeds 90\% and is associated with 5\% to 10\% risk of adverse events that include bile leak, perforation, and infection.\textsuperscript{59} The procedure requires advanced technical expertise and is best performed at tertiary-level endoscopy units (Fig. 14).

\textbf{Fig. 14.} EUS-guided cholangiogram reveals a long-segment biliary stricture in a patient with locally advanced pancreatic cancer. The patient underwent successful EUS-guided choledochoduodenostomy.
SUMMARY

EUS-FNA is the cornerstone of pancreatic tissue acquisition and is associated with excellent operating characteristics. The ability to reliably procure core tissue enables personalization of chemotherapy and improves clinical outcomes. In addition, EUS facilitates palliation of pain in pancreatic cancer and ablation of pancreatic cyst neoplasms. Biliary decompression at ERCP is successful in greater than 95% of patients with obstructive jaundice. However, EUS-guided biliary drainage is also becoming an effective rescue technique for palliation of jaundice when access to the bile duct is unsuccessful at ERCP.

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