Pancreatic and Biliary Endoscopy

William R. Brugge, M.D., and Jacques Van Dam, M.D., Ph.D.

Dramatic improvements in the quality of instrumentation have established endoscopy as the primary method for diagnosing and treating many pancreatic and biliary diseases. Endoscopic retrograde cholangiopancreatography (ERCP) is the most commonly used procedure in pancreatic–biliary endoscopy. Through its use of detailed endoscopic and fluoroscopic images, ERCP has evolved into a predominantly therapeutic technique. A new endoscopic procedure, endoscopic ultrasonography, provides high-resolution ultrasound images of the pancreas and biliary ducts and complements the findings of ERCP. With continued improvements in instrumentation, small-diameter catheters will permit even better imaging of the ductal systems with high-resolution endoscopy and ultrasonography.

Instrumentation

The duodenoscopes used for ERCP have two features that make them distinct from other endoscopes: they are side-viewing scopes, and they have the capacity to control the direction of catheters as they exit the instrument channel. The side-viewing feature provides imaging along the lateral aspect of the tip rather than from the end of the endoscope. This allows the endoscopist to obtain an image of the medial wall of the duodenum, where the ampulla of Vater is located. The entrance to the pancreatic and bile ducts contained within the ampulla of Vater is cannulated with specialized catheters placed through the instrument channel (Fig. 1).

An endosonoscope houses an ultrasound transducer in the tip of an endoscope. The transducer may be oriented in a radial or linear fashion. Linear-array endosonoscopes have the capacity to direct needle aspiration biopsies, a particularly important feature when evaluating the pancreatic–biliary system.

Small-diameter accessory instruments used in ERCP allow the endoscopist to cannulate and drain the pancreatic–biliary tree and to implant stents. Catheters, stents, and sphincterotomes are the basic tools used by endoscopists during ERCP, supplemented by baskets and balloons for the removal of stones. Cannulation is performed with small, tapered catheters designed to guide wires or injections of contrast medium into the pancreatic or biliary ducts. Stents are plastic or metal devices that can be placed across ductal stenoses to improve the flow of pancreatic or biliary secretions. The external drainage of bile and pancreatic juice can also be promoted by the placement of long catheters for drainage. Sphincterotomy of either the pancreatic or the biliary sphincter can be performed with a small catheter for cutting—a sphincterotome—to facilitate passage of a catheter or extraction of a stone.

In contrast to the indirect images obtained with fluoroscopy and ultrasonography, direct endoscopic images of the biliary and pancreatic ducts can be obtained through small choledochoscopes. These endoscopes are introduced through the instrument channel of a large-channel duodenoscope and passed into large ducts.

Biliary Diseases

Acute Cholangitis and Choledocholithiasis

One of the most common indications for biliary endoscopy is acute obstruction of the bile ducts, often by a stone, that is complicated by cholangitis. ERCP has become the preferred approach to the treatment of patients who are acutely ill with cholangitis because of its diagnostic and therapeutic capabilities. After biliary sphincterotomy, stones in the bile duct can be extracted with balloons or baskets pulled through the bile duct. In critically ill patients with sepsis, urgent biliary decompression can be accomplished without sphincterotomy by placing a small-diameter nasobiliary drain or an internal stent across the sphincter. Prompt drainage of the biliary tree in patients with cholangitis reduces the morbidity and mortality associated with biliary sepsis. Furthermore, drainage of the biliary tree with ERCP is associated with a lower rate of complications than surgical or transhepatic drainage.

The timing of ERCP in the treatment of patients with a biliary infection depends on the clinical presentation. In acute cholangitis, ERCP should be performed within 24 hours, because it has been found...
Figure 1. A Biopsy of a Pancreatic Mass Guided by Endoscopic Ultrasonography (Panel A) and the Placement of a Stent into a Malignant Bile-Duct Stricture with Endoscopic Retrograde Cholangiopancreatography (Panel B).
to improve the patient’s clinical course. Patients with suspected cholecoldolithiasis and no evidence of acute cholangitis may be evaluated less urgently, even if jaundice is present.

ERCP is the primary approach used for the treatment of patients with common-bile-duct stones. It is best reserved for patients who are very likely to have these stones, as determined by screening with laboratory tests and noninvasive imaging studies. Because bile-duct stones are difficult to detect by ultrasonography and computed tomography (CT), newer imaging tests have been developed that are more effective in the diagnosis of stones. Endoscopic ultrasonography is highly accurate in both detecting and ruling out the presence of bile-duct stones, and its use in patients with suspected stones is cost effective. The screening of patients with suspected bile-duct stones with these tests may decrease the need for diagnostic ERCP. Magnetic resonance cholangiopancreatography is also capable of identifying bile-duct stones but may not be as accurate as endoscopic ultrasonography. Patients who are undergoing laparoscopic cholecystectomy and are deemed unlikely to have cholecoldolithiasis on the basis of screening may undergo ERCP postoperatively if intraoperative cholangiography shows the presence of a stone in the bile duct.

Although extraction of small stones from the bile duct with ERCP is usually successful, extraction of large stones (larger than 1 cm) through a sphincterotomy may be difficult, and the stones may need to be fragmented in situ. Alternatively, if a stone cannot be removed, long-term stenting of the bile duct may result in dissolution of the stone. Fragmentation of stones in situ is performed by mechanical or electrohydraulic lithotripsy, followed by the removal of stone fragments with a balloon or a basket device. Cholecodochoscopy, the direct endoscopic examination of the bile duct, may improve the detection and fragmentation of complex stones. Concern has been expressed about the long-term effects of eliminating the function of the biliary sphincter as a result of sphincterotomy. Although some investigators report biliary infections and recurrent stones, others report few of these sequelae.

Acute cholecystitis resulting from obstruction of the cystic duct may complicate cholecoldolithiasis. Although ERCP is not commonly used in the treatment of patients with cholecystitis, it may be used to eliminate obstruction of the cystic duct through the placement of a stent into the duct. This technique has also been successfully used in patients with chronic obstruction of the cystic duct or acute acalculous cholecystitis.

**Benign Biliary Strictures and Bile Leaks**

Bile-duct strictures are a common cause of biliary obstruction and are usually evaluated and treated with ERCP. The most common causes of benign biliary strictures are surgical injuries, anastomotic stenoses, and primary sclerosing cholangitis. Although the underlying cause of a stricture may be suspected on the basis of CT findings, definitive diagnosis is usually made with ERCP. ERCP permits the aspiration of bile for culture, biopsy of the biliary mucosa, and cholangioscopy for the diagnosis of biliary infections or cancers that may complicate biliary strictures. The treatment of benign biliary strictures consists of graded dilation with catheters and balloons; the overall success rate of this treatment is 75 percent, a rate similar to that with surgical therapy. Endoscopic treatment of benign extrahepatic strictures in patients with primary sclerosing cholangitis often results in sustained improvement in liver function.

Bile leaks may result from surgery, trauma, or complications of procedures and can be successfully treated with sphincterotomy, placement of a biliary stent, or use of an endoscopically placed drainage catheter. Sphincterotomy, stent placement, or both eliminate resistance to flow in the bile ducts and promote biliary drainage into the duodenum. The temporary placement of a stent in the bile duct appears to be more effective than sphincterotomy alone but requires a second ERCP procedure for removal of the stent. Bile leaks may be complicated by obstruction by bile-duct stones, which are easily removed during ERCP. The long-term prognosis of postoperative bile leaks that are treated by endoscopic drainage is excellent.

Benign diseases of the ampulla of Vater may also cause chronic biliary obstruction because of abnormal contractions of the sphincter of Oddi or scarring of the ampulla. ERCP with manometric measurements of the pancreatic or biliary sphincters may reveal high sphincter pressures. However, the use of manometric measurements is associated with a high frequency of acute pancreatitis. The ablation of pancreatic or biliary sphincters with sphincterotomy is highly successful in relieving the symptoms associated with ductal obstruction but remains controversial in patients in whom the disorder is manifested only by abdominal pain. In fact, abdominal pain in patients with dysfunction of the sphincter of Oddi may be a result of sensitivity to duodenal distention rather than ductal obstruction.

**Malignant Biliary Obstruction**

ERCP plays a major part in the diagnosis and treatment of malignant biliary strictures. Cholangiocarcinoma should be suspected when an isolated irregular stricture is found with cholangiography. A tissue diagnosis of cholangiocarcinoma is usually attempted by obtaining cytologic specimens of the bile-duct mucosa or aspirated bile. However, the sensitivity of these techniques for detecting cancer is less than 75 percent. The availability of new tissue-sampling techniques or the use of cholecodochoscopy to view bile-
duct mucosa directly may increase the sensitivity of cytologic examination of biliary specimens.\textsuperscript{21,38}

Biliary stents that are placed with ERCP may be either plastic and temporary or metal and permanent. The placement of a plastic stent for intrahepatic or extrahepatic biliary cancer is effective in relieving biliary obstruction, but the effect is only temporary, lasting an average of one to three months before the stent occludes. The placement of stents reestablishes the flow of bile into the duodenum and ameliorates the symptoms of anorexia, pruritus, and jaundice, which are associated with biliary obstruction.\textsuperscript{39} Unfortunately, the lumen of the plastic stent often becomes obstructed by the growth of a biofilm (a layer of bacteria and mucin) on the surface, which necessitates the frequent replacement of the stent.\textsuperscript{40} Efforts to prevent the formation of biofilm and the occlusion of plastic stents have focused on trials of antibiotics and oral bile salts, but the results have been disappointing.\textsuperscript{41,42}

Because metal stents have larger diameters than plastic stents, they can maintain biliary decompression for an average of nine months.\textsuperscript{43} The higher cost of metal stents as compared with plastic stents is offset by a decrease in the frequency of stent replacement and the number of hospitalizations for biliary obstruction.\textsuperscript{44} When delivered by ERCP into the bile duct, a metal stent is constrained by a sheath; the wire mesh expands against the bile-duct wall when the sheath is retracted. Unfortunately, metal stents may also become occluded, often as a result of ingrowth of the tumor. The obstruction of a metal stent is best relieved by placing a plastic stent within the metal stent.\textsuperscript{45} Newly designed covered metal stents may offer improved patency.\textsuperscript{46}

Unresectable cholangiocarcinomas or gallbladder cancer can be palliated effectively with metal stents.\textsuperscript{47-49} Photodynamic therapy, a tissue-sensitizing technique that uses light to ablate malignant tissue, has proved effective in the biliary tree and improves the palliation obtained with use of metal stents.\textsuperscript{48} Although metal stents can be placed transhepatically, the endoscopic approach is preferred, because of its lower cost and ease of use.\textsuperscript{50}

Cancers of the ampulla of Vater are a rare cause of biliary obstruction; they are often diagnosed and, in some cases, treated by means of ERCP. The combination of distal biliary obstruction and an irregular enlargement of the ampulla suggests an ampullary cancer. Endoscopic ultrasonography can be used to determine the depth of malignant infiltration and to guide the approach to therapy.\textsuperscript{51,52} Patients with cancer confined to the duodenal mucosa can undergo snare electrocauterity of the tumor through ERCP or ablation with photodynamic therapy.\textsuperscript{53} Patients with a locally invasive malignant tumor should undergo pancreatoduodenectomy, whereas an unresectable or metastatic tumor can be palliated with placement of a stent across the obstructing neoplasm.

**PANCREATIC DISEASES**

Important recent developments in endoscopy have been improvement in the imaging of the pancreas and the treatment of pancreatic disorders. The ductal system of the pancreas can be imaged in detail with ERCP, whereas endoscopic ultrasonography permits detailed imaging of the parenchyma, ducts, and structures adjacent to the pancreas.\textsuperscript{54}

Congenital diseases of the pancreas can be diagnosed endoscopically. Cystic fibrosis, a relatively common disorder, rarely causes symptoms of chronic pancreatitis. However, the ductal system may be abnormal because of inspissated plugs obstructing the ducts. Latent cystic fibrosis in adults may be a cause of relapsing pancreatitis, but no distinguishing features of this disorder can be found with ERCP or endoscopic ultrasonography.\textsuperscript{55,56} Pancreas divisum is characterized by incomplete fusion of the ventral and dorsal pancreatic ducts.\textsuperscript{57} In this common congenital anomaly, most of the pancreatic secretions flow through the duct of Santorini and the minor ampulla rather than through the major ampulla. Inadequate emptying of the duct of Santorini in pancreas divisum may be a cause of acute or chronic pancreatitis. Interventions with ERCP that improve drainage from the duct of Santorini can reduce the severity and frequency of pancreatitis that is associated with pancreas divisum.\textsuperscript{58}

**Acute Pancreatitis**

A common cause of acute pancreatitis is choledocholithiasis. The presence of a stone may result in transient obstruction of the common channel shared by the pancreatic and bile ducts and result in acute pancreatitis. Although bile-duct stones can be extracted through a papillotomy with ERCP, whether such treatment actually provides clinical benefit to patients with acute biliary pancreatitis is controversial.\textsuperscript{59,60} Although the bile-duct complications of biliary pancreatitis, such as jaundice, are relieved by papillotomy and the extraction of stones, the pancreatitis may worsen.\textsuperscript{60} Furthermore, a common-bile-duct stone is found during ERCP in only 20 percent of patients with acute biliary pancreatitis; in most cases, the stone has been passed by the time ERCP is performed.\textsuperscript{61}

Acute relapsing pancreatitis may be caused by obstruction of the pancreatic duct as a result of disorders of the sphincter of Oddi, pancreatic ductal strictures, or pancreatic-duct stones. Patients who are likely to have an abnormality on the basis of the results of CT should undergo ERCP.\textsuperscript{62} Manometry of the sphincter of Oddi should be performed in patients suspected of having sphincter dysfunction. Focal and dominant strictures of the main pancreatic duct can be dilated or bypassed with a stent.\textsuperscript{63} Pancreatic stents are generally used only on a temporary basis, because the long-term presence of stents in the pancreatic duct often leads to ductal changes that resemble chronic pancreatitis.
Sphincterotomy of the pancreatic duct as a treatment for disorders of the pancreatic portion of the sphincter of Oddi can be performed safely when patency of the duct is ensured by the placement of a drain or stent. New treatments for dysfunction of the sphincter of Oddi include the intrasphincteric injection of botulinum toxin or nitric oxide. Endoscopic ultrasonography is useful in determining the cause of acute relapsing pancreatitis, because of its ability to detect ductal stones and masses, which are common causes of relapsing pancreatitis.

Chronic Pancreatitis

Chronic pancreatitis can be diagnosed with ERCP or endoscopic ultrasonography. The changes in the pancreatic duct due to chronic pancreatitis are readily identified by ERCP but are relatively nonspecific. For example, pancreatic infections in patients with the acquired immunodeficiency syndrome can simulate chronic pancreatitis. Although the late ductal changes of chronic pancreatitis may be apparent on CT, the early changes of focal dilatation, irregularities, and abnormal side branches may be seen only with ERCP. Parenchymal changes are best identified with endoscopic ultrasonography; they consist of focal calcification, tissue heterogeneity, small cysts, and abnormalities of the walls of the ducts. The early parenchymal changes of chronic pancreatitis precede functional changes in pancreatic secretion. ERCP and endoscopic ultrasonography probably complement each other in the diagnosis of chronic pancreatitis. However, endoscopic ultrasonography is less invasive than ERCP.

The endoscopic treatment of chronic pancreatitis is directed at relieving the focal obstruction of ducts caused by stones, strictures, or sphincteric disorders. Although evidence of obstruction is usually seen on ultrasonography or CT, more subtle evidence of obstruction of the pancreatic duct can be found by stimulating pancreatic secretion through the intravenous administration of secretin and observing dilatation of the duct with endoscopic ultrasonography. The endoscopic finding of dilatation of the pancreatic duct after stimulation by secretin has been used for disorders of the pancreatic portion of the sphincter of Oddi. The stones can be removed endoscopically or after they have been fragmented by lithotripsy; however, stones do not always need to be removed. The disruption of the pancreatic duct as a result of trauma may cause obstruction of the pancreatic duct and the formation of a pseudocyst; the obstruction can be treated with placement of a stent to bridge the duct at the disruption. In patients with sphincteric obstruction, pancreatic sphincterotomy can reduce the frequency of episodes of recurrent pancreatitis. In patients in whom there is no evidence of ductal obstruction, endoscopic ultrasonography can be used to direct injections to the celiac ganglia, which may provide relief of pain due to chronic pancreatitis.

In addition to ultrasonography and CT, either ERCP or endoscopic ultrasonography can be used to diagnose pancreatic pseudocysts. A pseudocyst may be seen on pancreatography if it fills with contrast medium. Pseudocysts should be treated if they are symptomatic or cause pancreatic or biliary ductal obstruction. Endoscopic treatment consists of drainage of the pseudocyst with a stent. The stent can be placed directly through the adjacent wall of the upper gastrointestinal tract or through the main pancreatic duct that communicates with the pseudocyst. Drainage through the pancreatic duct is highly successful but is possible only if the pseudocyst communicates with the main pancreatic duct. Transmural stent drainage of chronic pseudocysts is also successful if the wall of the pseudocyst is less than 1 cm in thickness.

As compared with radiologic approaches, an endoscopic approach to drainage of a pseudocyst permits internal drainage and does not require the use of external catheters. However, the placement of a pancreatic stent is complicated by infection and bleeding in 10 percent of patients. Endoscopic ultrasonography readily detects pancreatic pseudocysts and does not require injections of contrast medium into the pancreatic duct. Endoscopic ultrasonography is useful for selecting an appropriate site for stent placement with ERCP. Large-channel endosonoscopes can assist in the placement of a stent into a pseudocyst without requiring ERCP.

Pancreatic Tumors

Pancreatic islet-cell adenomas are benign tumors that can be diagnosed by endoscopic ultrasonography with an accuracy of more than 80 percent. Adenomas appear as round, isoechocic structures in the pancreas or adjacent lymph nodes. The use of endoscopic ultrasonography early in the evaluation of suspected adenoma is a cost-effective approach, and its use decreases the need for mesenteric angiography. The two most important clinical disorders associated with pancreatic islet-cell adenomas are the Zollinger–Ellison syndrome and hypoglycemia associated with insulinomas. Endoscopic ultrasonography...
locates more than 70 percent of insulinomas but may not locate extrapancreatic pedunculated lesions.\(^9\)

Gastrinomas are also readily detected by endoscopic ultrasonography, but the multifocal nature of the tumors and the high frequency of extrapancreatic locations make endoscopic ultrasonography less sensitive for detecting gastrinomas than insulinomas. When combined with upper endoscopy, endoscopic ultrasonography has an overall sensitivity of 60 percent for detecting gastrinomas.\(^9\) Endoscopic transillumination of the duodenum at exploratory laparotomy is the preferred method for locating duodenal gastrinomas, which constitute as much as 40 percent of gastrinomas.\(^9\) Endoscopic ultrasonography complements somatostatin-receptor scintigraphy in detecting pancreatic islet-cell adenomas, and the two tests should be used in the initial evaluation of patients with suspected gastrinomas and insulinomas.\(^94,95\)

The diagnosis and treatment of pancreatic cancers is an important use of ERCP and endoscopic ultrasonography. A malignant stricture of the pancreatic duct appears as an irregular narrowing of the main duct and may be associated with a distal biliary stricture. ERCP is very sensitive for detecting pancreatic cancer, but the finding of a ductal stricture is not specific to cancer.\(^96\) ERCP may also facilitate the diagnosis of cancer by providing tissue for cytologic examination and assay for various tumor markers.\(^37\)

Tumors of the head and body of the pancreas are most amenable to cytologic diagnosis with sampling by ERCP.\(^97\)

ERCP is often used to provide palliation in patients with pancreatic cancer by permitting the placement of a stent across an obstructed bile duct.\(^98\) Endoscopic stenting is superior to transhepatic stenting or surgical biliary drainage because of its high success rates and ease of placement.\(^98\) Long-term palliation is best achieved with endoscopically placed metal stents, because they decrease the need for hospitalization and ERCP.\(^44,99\) Stenting of the duodenum can also provide palliation in patients with pancreatic cancer.\(^100\) The rate of success of long-term palliation with biliary stenting is highest at centers that perform a high number of therapeutic ERCP procedures.\(^101\)

In the past, ERCP was used diagnostically if the CT findings were equivocal. However, the ability of endoscopic ultrasonography to detect pancreatic cancer through the finding of a focal hypoechoic mass may cause it to replace ERCP for the evaluation of suspected pancreatic cancer.\(^102\) Endoscopic ultrasonography is particularly useful for detecting small intra-pancreatic malignant tumors (those less than 3 cm).\(^103\) However, focal hypoechoic masses within the pancreas are not specific for cancer and can be found in patients with chronic pancreatitis. The use of pancreatic biopsy guided by endoscopic ultrasonography has substantially improved the ability of endoscopic ultrasonography to provide a definitive diagnosis of pancreatic cancer. A tissue diagnosis of pancreatic cancer can be achieved with sampling by this technique with accuracy rates of 85 to 95 percent.\(^104-106\)

Endoscopic ultrasonography can also provide information on the stage and location of tumors. The finding of vascular invasion into peripancreatic structures and the portal venous system is used to determine whether a mass is resectable.\(^107\) The use of endosonographic evidence of vascular invasion to determine the resectability of a tumor has a predictive accuracy rate of 80 to 90 percent, similar to rates achieved with angiography and CT.\(^108,110\) A recent study in which endoscopic ultrasonography was compared with spiral computed tomography for the staging of pancreatic cancer showed similar accuracy rates.\(^111\) Peritoneal and liver metastases that are not detected by computed tomography and endoscopic ultrasonography can be diagnosed with staging laparoscopy in as many as 29 percent of patients.\(^112\)

The diagnosis of cystic tumors of the pancreas offers the endoscopist the opportunity to treat an early form of pancreatic adenocarcinoma. More than 40 percent of pancreatic cystic tumors are malignant, and surgical resection offers a good prognosis.\(^113\) Although ERCP can be used to diagnose cystic neoplasms, which are indicated by the findings of ductal irregularities, cysts, and intraductal mucin, endoscopic ultrasonography can be used to identify and guide the biopsy of these treatable tumors.\(^114,115\) Cystic fluid can be aspirated for cytologic analysis and tumor markers that identify malignant cystic neoplasms.\(^116\)

Aside from chronic biliary obstruction, the other important complicaion of pancreatic cancer is pain. Biliary or pancreatic stenting rarely relieves the pain associated with pancreatic cancer. A blockade of the celiac ganglia performed surgically or radiologically is highly effective in reducing the pain and the need for narcotics. A blockade of celiac ganglia can be achieved under endoscopic guidance either temporarily with a local anesthetic or permanently with 98 percent ethanol.\(^117\) The advantages of endoscopic ultrasonography are its ease of use and low complication rate.

**COMPICATIONS OF ERCP AND ENDOSCOPIC ULTRASONOGRAPHY**

In contrast to most other endoscopic procedures, ERCP has a clinically significant complication rate. Although there may be bleeding or cholangitis in a small percentage of patients, these complications are rarely life-threatening. In contrast, pancreatitis or small retroperitoneal perforations as a complication of ERCP occur in 5 to 10 percent of patients and may result in considerable morbidity and mortality. Agents that have been used to reduce the frequency of pancreatitis include corticosteroids, somatostatin, and non-ionic contrast medium.\(^118-120\) Only a protease inhibitor has proved to be effective prophylactically.\(^121\) The use of a variety of new endoscopic techniques has re-
cently been shown to reduce the frequency of pancreatitis. More important, the rate of complications is related to the frequency and number of procedures performed by endoscopists. Endoscopic ultrasonography results in few complications. Bleeding and pancreatitis have been reported in up to 2 percent of patients undergoing pancreatic biopsy.

CONCLUSIONS
Pancreatic and biliary endoscopy have improved dramatically since they were introduced 25 years ago. ERCP is currently the test of choice in patients with choledocholithiasis. It can be performed without sphincterotomy for acute cholangitis. Gastrointest Endosc 1996;42:103-4.

REFERENCES


