Pancreatic cystic lesions are being identified more frequently due to the widespread use of state of the art imaging. Management of such lesions poses a conundrum due to the uncertainty of the behavior of these pancreatic cysts, which range from benign to malignant. The clinician must decide whether to resect or observe these lesions in view of current limitations in technology in tissue sampling techniques and in interpretation of the pathologic specimen, which often prevents the accurate characterization of the lesion. There are many factors involved in the decision of whether to observe or resect these lesions. If surgical resection is contemplated, there continues to be debate about the best surgical approach. Here we review the surgical approach to pancreatic cystic neoplasms.

**INTRODUCTION**

Pancreatic cystic neoplasms are encountered with increasing frequency as more sensitive imaging modalities are being performed for unrelated conditions.1 Cystic lesions can be broadly categorized into true cysts and false cysts. False cysts include pseudocysts and cystic degeneration of solid tumors. True cysts can be subdivided into non-neoplastic, such as congenital or lymphoepithelial cysts, and neoplastic cysts.1 Of the neoplastic cysts, the basic types are mucinous cystic neoplasms (MCN) and intraductal papillary mucinous neoplasms (IPMN).1 There are also the serous cystadenomas. It is rare for serous cystadenomas to undergo malignant transformation, while it is common for mucinous lesions to do so.2 Once a pancreatic cystic neoplasm is discovered, a management plan needs to be followed. The majority of pancreatic cysts can be managed nonoperatively.3,4 Those which are suspicious for being MCN’s or IPMN’s need a multidisciplinary approach.5,6 Management of pancreatic cystic neoplasms requires assessing the probability of the cysts malignant potential, the likelihood of operative complications, and the potential comorbidities that will result as a consequence of the resection.7 The latter two issues, operative complications and comorbidities, are directly impacted by the type of surgical procedure undertaken for resection.

(continued on page 17)
SURGICAL TREATMENT OF PANCREATIC CYSTS

Pancreatic Pseudocysts
Pancreatic pseudocysts occur following 5.1% to 16% of episodes of acute pancreatitis and are seen in 26% in patients with chronic pancreatitis. Because pseudocysts spontaneously resolve in 40% to 50% of patients treated expectantly with observation alone, observation is often appropriate given that the patient is asymptomatic. Traditionally, surgery has been recommended for pseudocysts larger than 6cm that persist over 6 weeks. More recent studies, however, have found that pseudocysts greater than 10cm in diameter may also resolve spontaneously. When evaluating pancreatic pseudocysts, understanding the pseudocyst relationship to the pancreatic ductal anatomy is key in predicting the success of continued observation versus the need for surgical intervention.

Intervention for pancreatic pseudocysts is warranted for symptomatic patients, for those that progressively increase in size, and if the cyst is infected. In addition, compression of major vessels (with manifestations such as ischemic pain, a positive hemoccult test due to ischemia, disturbed intestinal motility, or a rise in the serum lactate concentration), compression of the stomach or duodenum leading to clinical symptoms, stenosis of the common bile duct with impairment of biliary drainage, infection of the cyst, hemorrhage into the cyst, or a pancreaticopleural fistula, are all indications for intervention.

Percutaneous Drainage. Over the last several years’ modalities like percutaneous, endoscopic and laparoscopic drainage have gained interest. Percutaneous drainage is the least invasive method, though recent studies have shown successful drainage is achieved in only 40% to 60% of patients. In addition, an external drainage catheter needs to be in place for over 50 days. Compared to those undergoing surgery, percutaneously drained patients tend have higher complication and mortality rates and an increased hospital length of stay. Complications from percutaneous drainage requiring surgical intervention are also common and occur in 84%. Another disadvantage of percutaneous drainage is the inability to successfully remove all the necrotic debris. Therefore, percutaneous draining should be limited to patients with infected pseudocysts that require control of their sepsis prior to definitive surgical management.

Endoscopic Drainage. Endoscopic drainage of a pancreatic pseudocyst can be achieved transmurally, transpapillarily, or via a combination of both. The transpapillary approach is possible when the cyst communicates with the pancreatic duct, as occurs in 36% to 69% of patients. In this approach an endoscopic retrograde cholangiopancreatography is done to establish a patent communication between the pancreatic duct and the pseudocyst. Success rates of up to 100% have been reported. Possible complications of this procedure include pancreatitis, bleeding, scarring of the pancreatic duct and a biliary fistula. The transmural approach involves gaining access to the cyst cavity by traversing the wall of the stomach or duodenum. This may be aided using an endoscopic ultrasound (EUS) to visualize the cyst and its relationship to vascular structures. Recurrence rates of 5% to 20% have been reported. When EUS is not utilized, the pseudocyst must be in close proximity to the gastrointestinal wall (<1 cm) and there has to be a recognizable bulge from the pseudocyst into the stomach or duodenum. The success rate without EUS ranges from 70% to 100%. There are no obvious contraindications to EUS. However, it does carry a 3% to 13% risk of bleeding. Other possible complications include retroperitoneal perforation, cyst infection, and stent migration and clogging.

Surgical Internal Drainage. Surgical internal drainage is the mainstay of treatment. These operations include cystgastrostomy, cystoduodenostomy, or cystjejunostomy done either through a standard laparotomy or laparoscopically. The advantages of the surgical approach are that a larger stoma can be formed and necrotic debris can be evacuated. However, the disadvantages are that this approach may not be suitable for patients that are unable to tolerate general anesthesia, and it is clearly more invasive up-front. Surgical approaches for internal drainage are
largely determined by the anatomic location of the pseudocyst. All patients undergoing an open surgical procedure should also undergo a cholecystectomy if this has not been done previously.

For pseudocysts adherent to the posterior wall of the stomach, cystogastrostomy is easily accomplished. If the cyst is located in the head or unicate process of the pancreas, cystoduodenostomy might be preferred. For cysts not in proximity to the stomach or duodenum, Roux-en Y cystojejunostomy may be the best option. Cystogastrostomy is known to be simple, quick, and less prone to infection, but is more frequently associated upper gastrointestinal bleeding. There is no significant difference in cyst recurrence, morbidity, or mortality between cystogastrostomy and cystojejunostomy, but the operation is shorter and blood loss is less after cystogastrostomy.

Surgical Resection. Resection is an alternative procedure to internal drainage for chronic pseudocysts. Patients with severe pain due to chronic pancreatitis, those with multiple cysts, those who have had gastrointestinal hemorrhage, or those with bile duct or duodenal obstruction may require resection especially when it is not technically possible to drain the pseudocyst. Resection is done by utilizing a variety of different methods including partial left-sided pancreatectomy preserving the spleen if possible or by partial right-sided pancreatectomy that may or may not spare the duodenum.

Occasionally, internal drainage of pancreatic pseudocysts may be accompanied by primary drainage of the main pancreatic duct. This is necessary if there is ductal obstruction and can be accomplished using pancreaticocaudaloduodenectomy, a modification of the Peustow (Partington Rochelle procedure), Fry or Beger operations.

True Pancreatic Cysts

Enucleation. Enucleation of the pancreatic lesion refers to the surgical removal of the lesion in a non-anatomic fashion to preserve as much of the functional parenchyma as possible. In addition to preserving organ parenchyma, enucleation requires less operative time, is associated with less blood loss, and fewer complications. Prior to enucleation, a thorough preoperative and intraoperative evaluation must be conducted with enucleation performed only for benign pancreatic lesions. The size of the cyst and the absence of jaundice and vascular involvement on imaging studies are important factors in determining whether enucleation is an option. At the time of surgery, it is also essential to determine that no adjacent organs are involved. The entire cyst wall must be removed which can be difficult if there is local invasion or inflammation of the adjacent pancreas. Enucleation is the preferred treatment for insulinomas, gastrinomas in the duodenal wall or pancreas, pancreatic mucinous cystadenomas, and serous cystadenomas that require surgery.

One main disadvantage of enucleation over resection is that enucleation has a higher incidence of postoperative pancreatic fistulas. This can result in a longer hospital stay. In addition, careful observation for recurrence is required, since the long-term risk of recurrence is unknown.

Distal Pancreatectomy. The surgical procedure for benign or malignant lesions in the body or tail of the pancreas is the distal pancreatectomy. It involves removal of a portion of the pancreas to the left of the superior mesenteric/portal veins and does not include the duodenum or distal bile duct. The pancreas is usually divided to the left of the superior mesenteric/portal vein trunk, with the exact line of transection depending on the location of the lesion.

There are four primary variations of a distal pancreatectomy: open via a laparotomy or laparoscopically, with either an en bloc splenectomy or splenic-preserving techniques. Laparoscopic distal pancreatectomy has now become a standard operation in many centers. It is associated with less blood loss, a shorter time to oral intake, a shorter hospital stay, and a faster return to normal activity.

Traditionally, distal pancreatectomy has been done with an en bloc splenectomy due to division of the splenic artery and vein. Initial attempts at splenic preservation depended on preserving both the splenic artery and vein. In 1988, Warshaw described the technique of splenic preservation by dividing the splenic artery and vein, and conserving all of the short gastric vessels. Controversy exists regarding the
superiority of splenic preservation versus removal, and if the spleen is preserved, splenic vessel preservation versus division of the vessels.32

**Central Pancreatectomy.** Central pancreatectomy (CP) is a segmental pancreatic resection to remove benign or low-grade malignant tumors of the neck and proximal part of the body of the pancreas. The objective for CP is to remove the neoplasm, preserve functional parenchyma, and avoid a major resection. The exocrine secretions of the head and uncinate process of the pancreas drain through their normal path into the duodenum, while the distal pancreas drains into the gastrointestinal tract through either a pancreaticogastronomy or pancreaticojejunostomy.34 As a result, there is a reduced risk of diabetes and exocrine insufficiency, while the upper digestive and biliary anatomy is maintained with consequent digestive functions.35,36

**Pancreatoduodenectomy (Whipple).** The Whipple procedure is used for lesions located in the head or uncinate process of the pancreas. The operation involves the en bloc resection of the head and uncinate process of the pancreas, duodenum, common bile duct, gallbladder and the antrum of the stomach in the “standard” Whipple, but may preserve the pylorus in a “pylorus preserving” Whipple if this region is not involved by tumor. Although mortality rates have decreased, this operation still has a high complication rate.37

**Total Pancreatectomy.** IPMN’s are widely recognized as premalignant lesions. Their size and distribution within the pancreas has been proposed as a predictor of progression to malignancy. Lesions involving the main pancreatic duct more commonly have a malignancy associated with them at the time of resection than lesions arising from a branch duct. More importantly, in the main duct variant, the entire duct may be involved with the neoplasia. Therefore, in this setting, curative resection requires a total pancreatectomy.38 In patients with diffuse noninvasive disease, total pancreatectomy should be considered to minimize the chance of progression to invasive disease.

Total pancreatectomy involves resection of the entire pancreas, duodenum, common bile duct, gallbladder, and possibly the gastric antrum and the spleen. This results in all patients suffering from brittle insulin-dependent diabetes mellitus and pancreatic insufficiency.39

**PATHOLOGIC CONSIDERATIONS IN OPERATIVE CHOICE**

**Pancreatic Pseudocyst**

These inflammatory pseudocysts make up the majority of cystic lesions in the pancreas. These are more commonly associated with a history of acute or chronic pancreatitis or with a history of trauma. These are usually unilocular, have a thin wall (<4 mm) and rarely have internal septations. The fluid aspirated from an uncomplicated pseudocyst is thin and nonmucoid. Infected pseudocyst may produce purulent, mucoid-appearing fluid.

**Serous Cystadenoma**

Serous cystadenoma is commonly seen in women older than 60 years. A uniform distribution throughout the pancreas is seen. The cyst is composed of a cluster of microcysts (1 mm to 20 mm in size) with intervening septa. Its appearance resembles that of a “honeycomb.” Approximately 20% of serous cystadenomas are macrocystic, solid appearing and have a central scar. These are usually benign in nature, but serous cystadenocarcinoma rarely occur with only about 20 cases reported to date.1

**Mucinous Cystic Neoplasm (MCN)**

The benign mucinous cystadenoma is most often found in women 40 to 50 years of age. MCN have a tendency to form in the pancreatic body and tail. For the most part, they are usually unilocular and may consist of a few macrocysts, which typically measure >2 cm. When analyzing the contents of these lesions, mucin, hemorrhage, or debris are encountered. EUS aspirates can provide useful information when trying to distinguish the type of cyst present. Obtaining fluid analysis and cytology can aid in the decision process.

In the case of MCN, a carcinoembryonic antigen (CEA) level <192 ng/mL fails to support the presence of MCN, whereas values >192–200 ng/mL support the

(continued on page 22)
DISEASES OF THE PANCREAS, SERIES #1

Pancreatic Cystic Lesions

(continued from page 19)

interpretation of MCN, and >800 ng/mL is 98% specific for MCN and highly predictive of malignancy. Amylase levels are also helpful since amylase is typically very high and almost never <250 ng/mL in pseudocysts, and low in serous cysts.

One important factor is that MCNs do not communicate with the ductal system. The predominance toward the female gender arises from the mucin-secreting ovarian type stroma. The malignant cystadenocarcinoma tends to be large and may have thickened walls or septations. A peripheral eggshell calcification is highly predictive of cancer.

Intraductal Papillary Mucinous Neoplasm (IPMN)

Intraductal papillary mucinous neoplasms affect both genders equally. IPMN has a higher incidence in the sixth and seventh decades of life. These are found mostly in the head or body of the pancreas. An important distinguishing characteristic of an IPMN is that it does communicate with the ductal system. Furthermore, they lack an ovarian-type stroma. The IPMN can further be classified according to whether or not they communicate with the ductal system. The main-duct type (MDT-IPMN) and branch-duct type (BDT-IPMN) of IPMNs should be differentiated from each other. IPMNs are classified according to the degree of epithelial dysplasia, ranging from the benign adenoma to the borderline tumor, carcinoma in situ and infiltrative carcinoma. A higher incidence of malignancy in seen in MDT-IPMN. In MDT-IPMN, a dilatation >10–15 mm of the main pancreatic duct and a tumor size of >3 cm for BDT-IPMN is considered to herald malignant change. An identifying feature of MDT-IPMNs is that mucous is often seen extruding from the ampulla at the time of an ERCP.

Most PNETs are malignant except for insulinomas, of which the majority are benign. Functional PNETs include gastrinomas seen with Zollinger-Ellison syndrome, insulinomas, VIPomas, Somatostatinomas, and Glucagonomas. On imaging, these PNETs are typically hypervascular. Enucleation is an option for benign lesions like insulinomas. Most other procedures will depend on the location of the lesion will dictate the method of surgical resection. Serum markers for PNETs include pancreatic polypeptide and chromogranin A among others seen in the functional group. When elevated, they can help with the preoperative diagnosis and long-term follow-up of these patients.

Solid Pseudopapillary Tumor (Hamoudi Tumor)

Solid pseudopapillary tumors are a relative rare tumor. These are composed of cystic and solid elements. The pathogenesis within the pancreas is unclear. They are slow growing, and when large, can cause compressive symptoms. They are seen mainly in young women. Clinical and imaging features help differentiate them from other pancreatic neoplasms. These tumors have malignant potential. The biologic behavior of solid pseudopapillary tumors is less aggressive than that of many other pancreatic tumors and its prognosis is better if resected prior to malignant transformation. Surgical extirpation of the tumor will result in almost total survival (>95%) for those patients with tumors confined to the pancreas.

Management

An understanding of the various types of pancreatic cystic lesions is important in determining the treatment. Although a great amount of research has been done on this topic, management has yet to be standardized and is still evolving. Surgical resection is still usually required for pancreatic cystic lesions in symptomatic low risk patients. There are a variety of surgical options, which include pancreatectoduodenectomy, distal pancreatectomy, central pancreatectomy, total pancreatectomy, duodenal sparing pancreatic head resections, and enucleation.

For asymptomatic pancreatic cystic lesions, it is the malignant potential of the lesion that must be taken into

(continued on page 24)
account with specific patient factors related to potential morbidity of the procedure that determine the need for resection. Certain radiological features may predict malignancy in intraductal papillary mucinous neoplasm and mucinous cystic neoplasm. In addition, surgical resection is not only diagnostic but often therapeutic being the only definitive treatment in many cases. Moreover, all symptomatic patients merit some form of intervention. Surgery is recommended for a cystic lesion >3 cm, any cystic lesion associated with a solid component, or if the lesion is confirmed to be mucinous in nature. In MDT-IPMNs, surgical intervention is also advised due to their malignant potential. Likewise, surgical intervention is recommended for BDT-IPMNs that show malignant features including a main duct dilation to over 6 mm, a cyst size greater than 3 cm, mural bodies, or a positive cytology. The location of the lesion best guides the surgical procedure of choice.

Lesions in the head of the pancreas entail a pancreaticoduodenectomy. Although malignancy in serous cystadenoma is rarely reported, surgery is recommended for patients with symptoms, such as pressure effect. When they are located in the proximal pancreas, pancreaticoduodenectomy is often required. IPMNs have a predisposition for the pancreatic head, and again, often require a pancreaticoduodenectomy. It is important to obtain intraoperative frozen sections to confirm a negative surgical margin status to prevent recurrence. The pancreaticoduodenectomy procedure has complications associated with multivisceral organ removal. Although frozen sections are used routinely intraoperatively, they do have limitations and do not necessarily rule out lesions involving distant parts of the gland. It is found that up to 19% of IPMNs require total pancreatectomy for cure and a careful discussion should be held with the patient prior to this procedure due to its corresponding morbidity.

There are some who believe that IPMNs are a more generalized process and favor a total pancreatectomy, arguing that more localized resections would predispose to a greater risk of recurrence. The incidence of cancer found in specimens containing IPMNs has been reported between 7%–43%. The risks of total pancreatectomy, however, might outweigh its benefits and include both significant exocrine and endocrine dysfunction. Total pancreatectomy should not be a procedure of choice for IPMNs unless there are compelling circumstances such as a proven malignancy with positive margins or multifocal disease involving the entire gland. In the distal pancreas, mucinous cystic neoplasms are more common. These have malignant potential and should be resected.

As previously stated, MCNs have a predisposition to occur in the middle and distal pancreas. Historically the procedure of choice is a distal pancreatectomy with or without a splenectomy. Splenectomy associated with a distal pancreatectomy has been associated with some increased morbidity, more infective complications, and a longer hospital stay than distal pancreatectomy alone. Both procedures have a relatively low morbidity and mortality; however the long-term risks of diabetes are notable, with pancreatic insufficiently observed when 80% of the pancreatic function is lost or 12 cm of pancreas is resected. CP may be a better solution for non-malignant lesions.

CP offers an alternative to a distal pancreatectomy with the advantages of preserving pancreatic parenchyma, and at times, the spleen. In addition, in CP, more normal pancreatic tissue is preserved which helps prevent the sequelae of pancreatic insufficienty and diabetes from occurring. The major deterrent to the widespread use and acceptance of CP are higher anastomotic leak rates reported in the literature. Anastomotic leak rates following CP have been reported as high as 63%. CP by definition retains both the proximal remnant and the pancreaticoenteric anastomosis yielding two potential sources for leaking. With distal pancreatectomy, leak rates can be as high as 20% to 30%. There are studies that have shown lower leak rates. With pancreaticoduodenectomy leak rates have been reported between 10% to 15%. More data are sure to shine more light on CP in the future.

When performing surgical intervention, risks versus benefits and surgeon comfort and expertise will dictate the course. The operative procedures range from enucleation to total pancreatectomy.

References
Pancreatic Cystic Lesions

DISEASES OF THE PANCREAS, SERIES #1


