Evaluation and Management of Pancreatic Cystic Lesions

Case Study and Commentary, Linda S. Lee, MD

ABSTRACT

• **Objective:** To review the evaluation and management of pancreatic cystic lesions.
• **Methods:** Review of the literature in the context of a clinical case.
• **Results:** Pancreatic cysts are increasingly recognized due to the frequent use of abdominal imaging. Accurate characterization of these cysts is important not only to identify premalignant lesions that will require surgical resection, but also to allow conservative management of many cystic lesions that will not require surgery with its morbidity. Although reliable biomarkers are lacking, a wide spectrum of diagnostic tools are available to evaluate pancreatic cystic lesions, including radiologic, endoscopic, laboratory, and pathologic analysis.
• **Conclusion:** Pancreatic cysts present a challenge to clinicians. Integrating all available information combined with the patient’s characteristics offers the best approach to these at times confounding lesions.

Pancreatic cystic lesions increasingly present a clinical challenge. With technological advances and widespread utilization of radiologic imaging, these lesions are often identified incidentally. Recent radiology studies suggest pancreatic cysts are identified in up to 20% of magnetic resonance imaging (MRI) studies [1,2]. Unlike most hepatic and renal cysts, many pancreatic cystic lesions have malignant potential. Therefore, accurately distinguishing among them has important clinical implications.

Pancreatic cysts may be broadly classified into non-neoplastic cysts, cystic neoplasms, and necrotic degeneration of solid tumors. Nonneoplastic cysts have no malignant potential and include pseudocysts, retention cysts, benign epithelial cysts, and lymphoepithelial cysts. Cystic neoplasms include mucinous cystic lesions (mucinous cystic neoplasm [MCN] and intraductal papillary mucinous neoplasm [IPMN]) and nonmucinous lesions such as serous cystadenomas (SCA) (Table 1). Mucinous cysts are premalignant while nonmucinous lesions have low or no malignant potential.

Diagnosis of these lesions relies mainly on the combination of diagnostic imaging and analysis of cyst fluid obtained during endoscopic ultrasound-guided fine needle aspiration (EUS-FNA). Unfortunately, the imaging characteristics of pancreatic cysts can be similar, making differentiation between benign and premalignant lesions difficult [3,4]. In addition, current cyst fluid analysis techniques fail to clearly distinguish among the different types of pancreatic cysts as well as predict the behavior of these lesions [3,5]. The accurate classification of pancreatic cysts is important since premalignant lesions may require surgical resection, while others that are benign or indolent can be observed.

CASE STUDY

**Initial Presentation**

A 48-year-old female had gallstone pancreatitis 4 years previously at which time she underwent laparoscopic cholecystectomy and a 4.1-cm pancreatic cyst was identified in the tail of her pancreas, which was presumed to be a pseudocyst. This cyst was followed with serial abdominal computed tomography (CT) and recently was noted to be slightly larger at 4.7 cm.

**What is the differential diagnosis for the pancreatic cystic lesion?**

**Differential Diagnosis**

Previously pseudocysts were the most common pancreatic cystic lesion, while more recently they account for...
Pancreatic cystic lesions approximately one-third of pancreatic cysts [6]. About 50% to 60% of pancreatic cystic lesions are cystic neoplasms, which include mucinous cysts and SCAs, and cystic degeneration of solid neoplasms represents 10% of pancreatic cysts [6]. Nearly 90% of all pancreatic cystic neoplasms are the benign SCA and the premalignant or malignant mucinous lesions including MCN or IPMN [7].

Pseudocysts are sequelae of acute interstitial pancreatitis and require at least 4 weeks to form. A thin capsule formed of nonepithelialized granulation or fibrotic tissue forms a wall around amylase-rich fluid. Symptoms, when present, typically consist of abdominal pain. Gastric outlet and/or biliary obstruction may occur as well.

Serous cystadenomas are benign pancreatic cystic neoplasms, which very rarely become malignant. SCAs account for over 30% of pancreatic cystic neoplasms and typically occur in women over the age of 60 [8]. They arise anywhere throughout the pancreas with some studies suggesting higher incidence in the body and tail of the pancreas while others favor the head and neck. As with the majority of pancreatic cystic lesions, SCAs are often discovered incidentally. SCAs may present with nonspecific symptoms due to compression of adjacent organs by the cyst. Symptoms occur more commonly in larger cysts > 4 cm (77%) compared to cysts < 4 cm (22%). The most common symptom is nonspecific abdominal pain, with only about one-quarter of patients presenting with pain radiating to the back suggestive of pancreatic etiology.

The natural history of SCAs is not well described; however, they appear to grow over time. One study suggested that cysts smaller than 4 cm expand at a slower rate (0.12 cm/year) than cysts larger than 4 cm (1.9 cm/year) [9]. Malignant transformation is extremely rare with only a few case reports of serous cystadenocarcinoma. On pathology, SCAs are lined by glycogen-containing cuboidal epithelial cells (Figure 1).

Mucinous cystic neoplasms are premalignant parenchymal lesions that almost exclusively occur in women. They arise in the body and tail of the pancreas in approximately 95% of patients and are defined by the presence of ovarian-like stroma (Figure 2). Symptoms occur more commonly with MCNs than SCAs. Unlike SCAs, presence of symptoms in mucinous cystic lesions is associated with malignancy. Features concerning for malignancy in MCNs include older age, large size especially > 6 cm, and presence of thick cyst wall, mural nodules, or peripheral eggshell calcification [10]. The true incidence of malignancy in MCNs is unknown, although recent studies suggest lower rates (12% to 29%) of invasive cancer with only 5.5% carcinoma in situ [11].

IPMN is also a mucinous cyst that arises from the pancreatic ductal epithelium of the main duct, side branches, or both (Figure 3). It occurs more commonly in men between the ages of 50 and 60. While IPMNs usually arise in the head of the pancreas, they can occur anywhere in the pancreas as well as in multiple locations. There are 3 subtypes of IPMN: main duct (diffuse or segmental dilation of the main duct > 5 mm), branch duct (dilation of 1 or more side branches), and mixed type (both main duct and side branch involvement). By pathology, IPMN may also be classified as gastric, intestinal, or pancreaticobiliary type. Gastric type is typically low grade while the intestinal and pancreaticobiliary type

Table 1. Classification of Pancreatic Cysts

<table>
<thead>
<tr>
<th>Benign, Not Premalignant</th>
<th>Premalignant/ Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serous cystadenoma</td>
<td>Intraductal papillary mucinous neoplasm</td>
</tr>
<tr>
<td>Pseudocyst</td>
<td>Mucinous cystic neoplasm</td>
</tr>
<tr>
<td>Lymphoepithelial cyst</td>
<td>Solid pseudopapillary neoplasm</td>
</tr>
<tr>
<td>Lymphangioma</td>
<td>Cystic neuroendocrine tumor</td>
</tr>
<tr>
<td>Retention cyst</td>
<td>Metastatic cyst (eg, ovarian cystadenocarcinoma)</td>
</tr>
</tbody>
</table>

Figure 1. Histology of serous cystadenoma with a microcystic pattern. Cysts are lined by bland cuboidal cells with clear or palely eosinophilic cytoplasm.
types are more aggressive [12]. Interestingly, more recently, gastric type-IPMN that developed invasive adenocarcinoma was associated with worse survival than non-gastric-type IPMN with cancer [13]. While histological grading may hold some predictive value, this is currently only available following surgical resection.

Accurate differentiation among the clinical subtypes of IPMN is important due to differences in malignant potential and management. Differentiation into these subtypes usually occurs by radiology, however diagnostic accuracy of CT and magnetic resonance cholangiopancreatography (MRCP) compared to surgical pathology for branch duct (BD) and mixed type IPMN is 49% and 73%, respectively [14]. Nearly 20% of BD-IPMNs diagnosed by radiology are actually mixed type IPMN by surgical pathology [15]. Malignant potential of mixed type IPMN is believed comparable to main duct (MD)-IPMN.

MD-IPMN is characterized by dilation of the main pancreatic duct, usually due to a neoplasm in the proximal duct producing mucus that fills and dilates the entire duct. The risk of invasive cancer in MD-IPMN ranges from 40% to 50% [16]. Although main pancreatic duct dilation greater than 15 mm and presence of mural nodules have been associated with even greater rates of malignancy, malignancy is also present in up to 30% of asymptomatic patients with MD-IPMN without mural nodules or massive duct dilation. Alternatively, 35% of MD-IPMN followed conservatively for a median of 48 months did not develop malignancy in one study [17].

Approximately 15% of BD-IPMN can undergo malignant transformation [18]. Predictors of malignancy include presence of a mass, mural nodules, dilated main pancreatic duct, and cyst size greater than 3 cm, although some studies have demonstrated the presence of malignancy in smaller cysts. A recent study suggested that BD-IPMN growth of over 2 mm/year was associated with a 46% rate of malignancy compared to 2% malignancy in cysts growing slower than 2 mm/year [19]. Over long-term follow-up of median 59 months in BD-IPMN, the probability of developing pancreatic cancer at 5 years was 2.4% while at 10 years it jumped to 20% [20]. However, 70% to 90% of BD-IPMNs without mural nodules remain unchanged on median 33- to 61-month follow-up [21,22]. Interestingly, some studies suggest that BD-IPMN may indicate a premalignant condition of the entire pancreas as distinct pancreatic ductal adenocarcinomas have developed in 5.4% to 9.3% of patients with BD-IPMN [23,24].

Symptoms attributable to IPMN include steatorrhea and diabetes with 15% to 30% of IPMNs presenting with
Pancreatic Cystic Lesions

Acute pancreatitis, which is believed to be due to obstructive pancreatitis from mucus plugging the ducts. Most patients undergo recurrent episodes of mild pancreatitis before diagnosis of IPMN. Rates of pancreatitis related to IPMN do not appear to be affected by cyst size, type of IPMN, or presence of malignancy [25].

Other less common pancreatic cystic neoplasms include solid pseudopapillary neoplasm (SPEN), which occur almost exclusively in young women. SPENs account for 1% to 2% of pancreatic cystic neoplasms. They were first described in 1959 as Frantz or Hamoudi tumors and then renamed SPEN by the World Health Organization in 1996. About 10% to 15% of SPENs are malignant, and to date, no predictors of aggressive behavior have been identified [26]. These patients usually present with nonspecific abdominal pain and occasionally with an abdominal mass palpable on examination. SPENs may occur anywhere throughout the entire pancreas. Pathology reveals characteristic pseudopapillae with cystic spaces containing hemorrhage and cholesterol clefts in myxoid stroma alternating with solid tissue.

Less commonly observed lesions such as neuroendocrine or acinar cell tumors can occasionally undergo cystic degeneration. Cystic neuroendocrine tumors account for only 8% to 17% of pancreatic neuroendocrine tumors and are usually nonfunctional [27]. Acinar cystadenocarcinoma is extremely rare, with fewer than 10 cases reported in the literature, and typically presents with abdominal pain and a multicystic lesion [28].

Rare nonneoplastic pancreatic cysts include pancreatic lymphangioma, which is an endothelium-lined cyst arising from the lymphatic system due to blocked lymphatics from inflammation or congenital anomaly [29]. During embryogenesis, ectopic lymphatic tissue lands in the pancreas and these cysts form from progressive dilation of insufficiently draining lymphatic vessels. Most pancreatic lymphangiomas occur incidentally in women in the body and tail of the pancreas. Complications include abdominal pain, hemorrhage, infection, and hydronephrosis.

Lymphoepithelial cysts are another group of rare nonneoplastic pancreatic cysts accounting for 0.5% of pancreatic cysts [30]. These typically occur in middle-aged men in the body or tail of the pancreas. The cysts lined by stratified squamous epithelium with subepithelial lymphoid tissue and follicles. The equally rare simple or true cyst is lined by cuboidal epithelial cells and does not communicate with the pancreatic duct. They occur in about 10% of patients with autosomal-dominant polycystic kidney disease. In addition, they are the most common pancreatic lesion seen in up to 72% of patients with von Hippel-Lindau disease [31].

Retention cysts are actually cystically dilated segments of pancreatic duct resulting from obstruction [30]. The obstruction may result from stones or stricture from chronic pancreatitis or cancer. Viscous mucus in cystic fibrosis may also clog the pancreatic duct.

Case Continued

The patient was referred for endoscopic ultrasound with the following findings: 3.7-cm thick-walled unicocular cyst in the tail of the pancreas without a solid component or mural nodule. The main pancreatic duct upstream from the cyst was dilated to 2.4 mm while the rest of the pancreatic duct was normal caliber. Fine needle aspiration (FNA) revealed the following: carcinoembryonic antigen (CEA) 304.9 ng/mL, amylase 30630 U/L, cytology with no malignant cells. DNA analysis revealed no k-ras or loss of heterozygosity mutations.

What diagnostic tools are available to evaluate pancreatic cystic lesions?

Differentiating among pancreatic cystic lesions and predicting malignant transformation can prove challenging. Current evaluation of pancreatic cysts includes a combination of radiologic imaging, endoscopic ultrasound, and cyst fluid analyses. For radiologic characterization of pancreatic cysts, patients should undergo a “pancreatic protocol” abdominal CT scan and/or MRI [32]. The multidetector CT should be dual-phase contrast-enhanced with images acquired during the pancreatic and portal venous phases which can be analyzed in 3-D. MRI images should be obtained at 1.5 or 3 Tesla with T1, T2, and 3-D, fat-saturated, gradient-echo T1 gadolinium-enhanced sequences in pancreatic, portal, and equilibrium phases with MRCP. Recent consensus by radiologists recommended MRI as the preferred imaging modality with its enhanced ability to detect septa, nodules, and ductal communication [32]. MRCP is superior to CT in characterizing IPMN by demonstrating ductal communication, main duct involvement, and small branch duct cysts [33]. Furthermore, recent concern over radiation exposure from repeated CT may favor the use of MRI for surveillance of pancreatic cysts.
Overall accuracy of radiologic imaging for the histologic diagnosis of pancreatic cysts is about 40% to 60% [35–37]. Both CT and MRI predict the presence of malignancy in pancreatic cysts more accurately (73% to 79%) [32,38]. The radiologic imaging features which may be helpful or diagnostic of various pancreatic cystic lesions as well as the presence of malignancy in them are described below.

SCAs are typically multicystic with each cyst < 2 cm, and 30% have a lobular “honeycomb” appearance due to dense septations, producing multiple small cysts (Figure 4). Up to 10% of SCAs may be unilocular or contain few septa, making differentiation from MCN difficult [8]. Occasionally these lesions may appear solid due to the presence of numerous microcysts that give the appearance of a homogeneous hypoechoic mass. The pathognomonic central scar or “sunburst calcification” is present in only about 30% of these cysts (Figure 5) [39].

Unlike SCA, MCNs usually appear smooth, well-defined, and unilocular or with a few septations (Figure 6). Thick septae, asymmetric wall thickening, mural nodules, and calcifications are associated with malignancy [10]. Calcifications within the peripheral wall of the cyst and occasionally in the cyst content occur in less than 20% of MCNs. Without a clear history of acute or chronic pancreatitis, differentiation of MCN and even SCA and BD-IPMN from pseudocysts may be difficult by imaging alone. On abdominal CT pseudocysts typically appear round with a thin or thick wall. Calcifications and communication with the pancreatic duct may be present.

IPMNs are ductal lesions involving the main pancreatic duct, side branches, or a combination of both. MD-IPMNs lead to diffuse dilation of the main pancreatic duct (Figure 7). Diagnosis of BD-IPMN relies on demonstrating communication of the affected side branch with the main pancreatic duct (Figure 8). Approximately 20% of BD-IPMNs diagnosed by radiology are actually mixed type IPMN by pathology [14]. This is clinically important because mixed type
IPMN has a malignant potential similar to MD-IPMN, and thus, surgical resection is recommended for these lesions [40].

Unlike most other pancreatic cystic lesions, SPEN and cystic neuroendocrine tumors usually have characteristic findings on imaging. The rare SPEN typically presents as a large well-defined encapsulated mass with a peripheral solid component and cystic degeneration in the center with areas of hemorrhage (Figure 9) [41]. Peripheral calcification is present rarely. Cystic neuroendocrine tumors are highly vascularized with early enhancement of the rim during early arterial imaging with CT (Figure 10 and Figure 11) [27]. Lymphangiomas are difficult to distinguish from pancreatic cystic neoplasms on imaging and typically appear multiseptate and well-defined [29].

The diagnostic rates of radiology are comparable to endoscopic ultrasound imaging with 51% accuracy for diagnosing mucinous lesions [42]. MRI and EUS may be complementary techniques with the use of both potentially increasing diagnostic yield for mucinous cysts [43]. Both MRI and EUS have modest sensitivity (58% to 67%) for detecting mural nodules. A recent study defined
EUS criteria for differentiating mucus from a nodule, and training in the detection of these EUS criteria improved diagnostic accuracy from 57% to 79% [44].

Diagnosis of MD-IPMN specifically may be aided by other endoscopic procedures including endoscopic retrograde cholangiopancreatography (ERCP) with pancreatoscopy and intraductal ultrasound (IDUS). Endoscopic visualization of mucin emerging from the major or minor papilla is pathognomonic for MD-IPMN (Figure 12). On ERCP, findings consistent with MD-IPMN include diffuse or segmental pancreatic duct dilation with filling defects. Pancreatoscopy, which involves direct endoscopic visualization within the pancreatic duct using special instruments, can be helpful in differentiating MD-IPMN from chronic pancreatitis by visualizing intraductal tumor [45–47]. Similarly IDUS with the insertion of a tiny ultrasound probe into the pancreatic duct can aide in diagnosis of MD-IPMN with identification of the frond-like tumor within the duct [48].

Often imaging alone, whether by radiology or EUS, is inadequate to accurately characterize pancreatic cystic lesions. With advances in endoscopy allowing the safe sampling of pancreatic cyst fluid during EUS [49], FNA of pancreatic cysts may be performed to analyze cyst fluid for various biochemical markers, DNA markers, and cytology. Cytology is generally nondiagnostic with most studies demonstrating less than 50% sensitivity for diagnosis of the lesion [50–53]. Cyst fluid from SCA, MCN, and IPMN is generally acellular or paucicellular. Cytology at best is able to differentiate mucinous from serous cystic lesions. Diagnostic yield of cytology is higher for SPEN and possibly cystic neuroendocrine tumors. A multicenter study of patients with histologically proven SPEN demonstrated EUS-FNA cytology accuracy of 75% [54]. Similarly, EUS-FNA of pancreatic lymphangiomas may be diagnostic in the presence of chylous-appearing cyst fluid, elevated triglyceride, and numerous benign lymphocytes [55,56].

Few cyst fluid markers have proven valuable and none are diagnostic (Table 2 and Table 3). CEA has been most extensively studied and is used to differentiate mucinous from non-mucinous cystic lesions. Elevated CEA level is consistent with a mucinous cyst, but the cutoff level remains debated, with studies using varying levels from 110 to 800 ng/mL [57]. In addition, CEA cutoffs can vary depending on the laboratory performing the assay. The higher the CEA, the greater the specificity while sensitivity is sacrificed. The commonly used cutoff of 192 ng/mL yields modest sensitivity (73%) and specificity (84%) [58]. Low CEA less than 5 ng/mL is 95% specific for a SCA or pseudocyst. Cyst fluid amylase lower than 250 U/L excludes a pseudocyst with 98% specificity and 44% sensitivity [57]. A recent study concluded that serum biomarkers may be helpful in predicting malignancy within IPMN [59]. This study of surgically resected

---

**Figure 11.** EUS of pancreatic cystic neuroendocrine tumor appearing well-defined, heterogeneous with solid and cystic components.

**Figure 12.** “Fish mouth” papilla on ERCP with mucin at major papilla.
Pancreatic cystic lesions

IPMN found that elevated serum CA 19-9 and CEA levels were predictive of invasive carcinoma in IPMN. More recent interest has focused on molecular DNA markers in cyst fluid to diagnose malignant pancreatic cystic lesions. A multicenter study suggested high specificity (96%) for malignancy when k-ras mutation was followed by allelic loss, but very low sensitivity (37%) [60]. This pattern of mutations had perfect specificity for diagnosing a mucinous cystic lesion but only 19% sensitivity. Presence of k-ras mutation alone had 96% specificity and 45% sensitivity for detecting mucinous lesions.

Table 2. Laboratory Markers and Pancreatic Cysts

<table>
<thead>
<tr>
<th>Type of Cyst</th>
<th>CEA</th>
<th>Amylase</th>
<th>Cytology</th>
<th>k-ras</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudocyst</td>
<td>↓</td>
<td>↑</td>
<td>Cyst content</td>
<td>–</td>
</tr>
<tr>
<td>SCA</td>
<td>↓</td>
<td>↓</td>
<td>Hemosiderin-laden macrophages</td>
<td>–</td>
</tr>
<tr>
<td>MCN</td>
<td>↑</td>
<td>↓</td>
<td>PAS+ cuboidal epithelial cells</td>
<td>+</td>
</tr>
<tr>
<td>IPMN</td>
<td>↑</td>
<td>↑</td>
<td>Mucinous cells</td>
<td>+</td>
</tr>
</tbody>
</table>

Table 3. Diagnostic Markers for Pancreatic Cysts

<table>
<thead>
<tr>
<th>Marker</th>
<th>Sensitivity</th>
<th>Specificity</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cytology</td>
<td>32%</td>
<td>100%</td>
</tr>
<tr>
<td>CEA &lt; 5 ng/mL (SCA or pseudocyst vs. mucinous lesions)</td>
<td>54%</td>
<td>94%</td>
</tr>
<tr>
<td>CEA &gt; 192 ng/mL (mucinous vs. nonmucinous lesions)</td>
<td>73%</td>
<td>84%</td>
</tr>
<tr>
<td>Amylase &lt; 250 U/L (SCA, MCN vs. pseudocyst)</td>
<td>44%</td>
<td>98%</td>
</tr>
<tr>
<td>k-ras mutation + allelic loss (malignant vs. nonmalignant)</td>
<td>37%</td>
<td>96%</td>
</tr>
</tbody>
</table>

- What are the management options for pancreatic cystic lesions?

Management of each type of pancreatic cystic lesion is defined and will be discussed below (Figure 13). Uncertainty remains over the best long-term management of small pancreatic cysts, which often have no definite diagnosis, as well as the management of known small BD-IPMN, MCN and early MD-IPMN with the lack of adequate natural history data for these lesions. SCAs are typically followed with serial imaging due to their tendency to grow, although the frequency of imaging is debatable, with some advocating imaging every 12 months while others suggest biennial surveillance [61–63]. Because these are benign lesions, surgical resection is reserved for patients with symptoms, cystic lesions without a clear diagnosis, and potentially large (> 4 cm) lesions.

On the other hand, the premalignant nature of MCNs combined with the inability to diagnose malignancy reliably in MCNs preoperatively and the relatively younger age of these patients drives consensus recommendations for surgical resection of all these lesions. Patients who are poor surgical candidates may be followed [64]. Patients with invasive adenocarcinoma arising from an MCN have relatively poor 5-year survival (15% to 57%) with recurrence rate of 37%, although this survival is far higher than non-MCN-associated pancreatic adenocarcinoma [64]. These patients should have ongoing radiologic follow-up after resection, while patients without histologic evidence of invasion do not require this. The 5-year survival for patients with noninvasive MCN is 100%.
Similarly, surgical resection is recommended for all patients with main duct and mixed type IPMN. Careful follow-up may be feasible in a select group of patients with no symptoms, mural nodules, or increase in pancreatic duct size as well as main pancreatic duct less than 10 mm. A small longitudinal study reported that malignancy developed in 20% of patients with MD-IPMN during median 49-month follow-up [17]. All these patients had evidence of progression in pancreatic duct dilation, while the others without malignancy had stable pancreatic duct dilation. Similar to MCN-associated cancer, IPMN-related invasive adenocarcinoma has a favorable 5-year survival (34% to 62%) compared to pancreatic ductal adenocarcinoma (9% to 21%) [66,67].

![Algorithm for management of different pancreatic cysts](image)

**Figure 13.** Algorithm for management of different pancreatic cysts. BD = branch duct; ERCP = endoscopic retrograde cholangiopancreatography; EUS = endoscopic ultrasound; FNA = fine needle aspiration; IPMN = intraductal papillary mucinous neoplasm; MCN = mucinous cystic neoplasm; MD = main duct; PD = pancreatic duct; SCA = serous cystadenomas; SPEN = solid pseudopapillary neoplasm. *High-risk features = solid mass, nodule, main pancreatic duct ≥ 1 cm, thick pancreatic duct wall, intraductal mucin or nodule, cytology suspicious or positive for malignancy.*
BD-IPMN may be followed conservatively or surgically resected depending on presence of features concerning for malignancy. Revised International Association of Pancreatologia (IAP) consensus criteria recommend surgical resection of BD-IPMN in patients with obstructive jaundice and a cystic lesion in the head of the pancreas, solid component, main pancreatic duct > 10 mm, mural nodule, main duct involvement (thickened wall, mural nodule or intraductal mucin), or cytology suspicious or positive for malignancy [64]. The previous criteria from 2006 also supported surgery for cyst size > 3 cm [16]; however, the recent criteria de-emphasize size as the sole criteria in the decision to operate and indicate to “strongly consider” surgery in young, otherwise healthy patients with cysts > 3 cm. The negative predictive value of the initial IAP guidelines for surgical resection of BD-IPMN was 100% in three different studies [68–70]. Another study applied the 2006 IAP guidelines to all pancreatic cystic lesions and found a lower negative predictive value of 86% [71]. The positive predictive value is very low at approximately 14% to 22%. Therefore, while following the initial IAP guidelines will enable physicians to identify most BD-IPMN that can be followed without surgical resection, many patients will undergo unnecessary surgical resection.

The revised IAP guidelines recommend further evaluation with EUS in patients with pancreatitis or one of the following on initial radiology (CT or MRI with MRCP): cyst size > 3 cm, thickened cyst wall, mural nodule, main pancreatic duct 5–9 mm, abrupt change in the main pancreatic duct caliber with atrophy in the upstream pancreas, or lymphadenopathy. Patients who do not undergo surgical resection should be followed with surveillance imaging. A repeat CT or MRI with MRCP should occur 3–6 months following the initial imaging. If the lesion appears stable, surveillance recommendations depend on cyst size ranging from every 3–6 months for cysts > 3 cm to every year or other year for cysts < 2 cm.

All patients with SPEN should undergo surgical resection. Presence of local invasion or limited metastases is found in less than 20% of patients with SPEN and is not a contraindication to surgical resection. Long-term survival is excellent for these patients with 5-year survival rates of 95% [72]. Patients with pancreatic lymphangioma may be followed or undergo surgical resection for symptoms or complications [29].

The guidelines outlined above for the various types of cysts require the ability to definitively diagnose the pancreatic cyst. Unfortunately, a major problem with managing pancreatic cystic lesions is that often despite extensive radiologic and endoscopic evaluation, the diagnosis of the lesion remains uncertain [15]. A longitudinal study with mean 4-year follow-up examined the rate of malignancy in incidental pancreatic cystic lesions that were not initially referred for surgical resection with 96% diagnostic indeterminacy following both radiologic and EUS-FNA evaluation [73]. Only one patient developed a mucinous cystadenocarcinoma at 7-year follow-up. Figure 14 illustrates an algorithmic approach to incidental, indeterminate pancreatic cystic lesions.

A decision analysis of asymptomatic patients with incidentally discovered pancreatic cystic lesions factored in the patient’s age, cyst location, cyst size, and American Society of Anesthesiologists score to assess the most cost-effective approach to these patients [74]. Three management options were evaluated: conservative with radiologic follow-up, aggressive with surgical resection for all surgical candidates, and an EUS-directed approach. The latter was the most cost-effective strategy with decision for radiologic follow-up or surgery based on a combination of cytology and CEA from EUS-FNA in addition to the patient’s surgical risk.

Case Follow-up

Diagnostic studies concluded the patient had either a MCN or mixed type IPMN. Surgical resection is recommended for both lesions, and this patient was a young, good surgical candidate. The patient underwent distal pancreatectomy without complications, and surgical pathology was consistent with a MCN with low-grade dysplasia.

CONCLUSION

The majority of pancreatic cystic lesions are cystic neoplasms and cystic degeneration of solid tumors. Pancreatic cystic lesions present a challenge to clinicians due to their increased incidental identification on radiology imaging and the limitations of currently available diagnostic tools. Following initial identification of a pancreatic cystic lesion, a dedicated pancreatic abdominal CT scan or MRI pancreas with MRCP should be performed. Surgical resection is recommended for all surgical candidates with MD-IPMN, mixed type IPMN, mucinous cystic neoplasm, and solid pseudopapillary neoplasm. Serous cystadenoma may be followed with serial imaging unless the patient develops symptoms or the diagnosis of
Figure 14. Algorithm for management of asymptomatic incidental pancreatic cysts.
the lesion is unclear. Surveillance is also recommended for BD-IPMN without the following features concerning for potential malignancy: obstructive jaundice and a cystic lesion in the head of the pancreas, solid component, main pancreatic duct > 10 mm, mural nodule, main duct involvement (thickened wall, mural nodule or intraductal mucin), cytology suspicious or positive for malignancy. BD-IPMN > 3 cm without the concerning features may also be followed carefully, although surgical resection should be strongly considered in young, surgically fit patients. A combination of radiologic imaging with EUS-FNA, cytology, CEA, amylase, and DNA markers may be used for diagnosis of pancreatic cystic lesions. An EUS-guided approach for deciding surgical resection versus radiologic surveillance may be the cost-effective approach in these patients.

Corresponding author: Linda S. Lee, MD, 75 Francis St., Boston, MA 02115.

Financial disclosures: None.

REFERENCES

Pancreatic Cystic Lesions


