Diagnosis and Management of Cystic Pancreatic Lesions

OBJECTIVE. The purpose of this review is to outline the management guidelines for the care of patients with cystic pancreatic lesions.

CONCLUSION. The guidelines are as follows: Annual imaging surveillance is generally sufficient for benign serous cystadenomas smaller than 4 cm and for asymptomatic lesions. Asymptomatic thin-walled unilocular cystic lesions smaller than 3 cm or side-branch intraductal papillary mucinous neoplasms should be followed up with CT or MRI at 6 and 12 months interval after detection. Cystic lesions with more complex features or with growth rates greater than 1 cm/year should be followed more closely or recommended for resection if the patient’s condition allows surgery. Symptomatic cystic lesions, neoplasms with high malignant potential, and lesions larger than 3 cm should be referred for surgical evaluation. Endoscopic ultrasound with fine-needle aspiration (FNA) biopsy can be used preoperatively to assess the risk of malignancy.

Clinical Vignettes and Images
The increasing use and improved spatial and contrast resolution of advanced cross-sectional imaging techniques such as MDCT and MRI have resulted in a marked increase in the incidental detection of cystic pancreatic lesions. They are encountered in as many as 2.6% of abdominal MDCT examinations and 20% of MRI studies [1–3]. Larger cystic pancreatic lesions are typically symptomatic, and incidentally detected cystic pancreatic lesions are often small. Increased identification of cystic pancreatic lesions at MDCT and MRI presents a clinical conundrum for appropriate further management [4–7]. Accurate characterization of these cystic lesions is essential for further management, either surgical or conservative. In a select group of patients, endoscopic ultrasound and cyst aspiration can be performed for further characterization. Clinical vignettes are presented in Figures 1–4.

The Imaging Question
How do we characterize, diagnose, and appropriately manage incidentally found cystic pancreatic lesions?

Background and Importance
Cystic pancreatic lesions encompass a varied group of pancreatic abnormalities, including inflammatory (pseudocysts), benign (serous cystadenomas), precancerous (intraductal papillary mucinous neoplasms [IPMNs] and mucinous cystic neoplasms [MCNs]), and frankly malignant (cystadenocarcinomas) [8–12]. Cystic pancreatic lesions not only have diverse histologic and imaging appearances but also differ in clinical presentation, biologic behavior, growth pattern, and risk of malignancy (Table 1). Accurate risk stratification and decisions on treatment and follow-up strategy necessitate precise lesion characterization and diagnosis [2, 13–16]. The current management of common cystic pancreatic lesions is summarized in Table 2.

Synopsis and Synthesis of Evidence
The most common nonneoplastic cystic pancreatic lesions are pseudocysts, which usually arise as a sequel of pancreatitis or trauma. The most common cystic pancreatic neoplasms are IPMNs, MCNs, and serous cystadenomas (SCAs) [12, 17–20]. Although SCAs and pseudocysts are considered benign, IPMNs and MCNs have malignant potential [19, 21–23]. Other cystic pancreatic lesions account for fewer than 10% of cases and include uncommon pathologic findings such as solid pseudopapillary neoplasms, cystic pancreatic neuroendocrine neoplasms, cystic degeneration in other solid pancreatic neoplasms, lymphoepithelial

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cysts, and cystic adenocarcinoma of the pancreas [5, 24, 25].

**Diagnosis**

Imaging plays a crucial role in the management of cystic lesions of the pancreas, including lesion detection and characterization. Technologic innovations in MDCT and MRI have led to improvement in analysis and morphologic differentiation of cystic pancreatic lesions and are widely considered the primary imaging modalities in the care of patients with cystic lesions of the pancreas. In addition, advances in postprocessing have enabled enhanced definition of the extent of a lesion and its relation to adjacent structures. These techniques are particularly valuable in delineating the relation between the cystic lesion and the pancreatic duct, a key feature in differentiating side-branch IPMNs from other cystic lesions [24, 26, 27]. The following imaging modalities can be used either independently or in combination to help in the diagnosis and management of cystic pancreatic lesions.

**MDCT**

MDCT is the primary modality for imaging of cystic pancreatic lesions, including IPMNs, owing to its high spatial and temporal resolution, speed of acquisition, wide availability, and ease of interpretation [2, 15, 16, 28]. The superior quality of 2D and 3D image displays generated from isotropic MDCT datasets has facilitated excellent depiction of the detailed regional pancreatic anatomy and precise definition of the morphologic characteristics of cysts [26, 29, 30]. Image postprocessing in a desired plane also allows determination of the communication between the cystic lesion and the main pancreatic duct, a key feature in the diagnosis of side-branch IPMNs [26]. However, the presence of a small duct or a collapsed duct can impede visualization of ductal communications [26].

MDCT has a reported accuracy of 56–85% for characterization of cystic pancreatic lesions, which is comparable to that of MRI [2, 15, 16, 28, 31]. Visser et al. [30] found that MDCT had an accuracy of 76–82% in establishing the diagnosis of malignancy in 58 histopathologically proven cystic pancreatic masses. In a study of 100 cystic pancreatic lesions, Chaudhari and colleagues [32, 33] reported an accuracy of 71–79% for MDCT for discriminating premalignant or malignant lesions from benign lesions. Lee et al. [2] reported a comparable accuracy (63.9–73.5%) of MDCT for differentiating benign from malignant cystic pancreatic lesions. However, subclassification of cystic lesions into histopathologic types is often difficult because of overlapping imaging features. Increasingly, the morphologic pattern depicted on MDCT images is being used to categorize cystic pancreatic lesions broadly into mucinous and nonmucinous types and then subdivide them on the basis of complex features into aggressive and nonaggressive lesions [2, 15, 22]. In a study of 114 patients with 130 cystic pancreatic lesions, Sahani and colleagues [15] stratified the lesions into mucinous and nonmucinous subtypes with an accuracy of 82–85% and reported an accuracy of 85–86% for recognizing aggressive biologic features. Similar accuracy has
been reported for small cystic pancreatic lesions (≤ 3 cm). Sainani et al. [16] found that MDCT had 71–84.2% accuracy for differentiating mucinous and nonmucinous subtypes of small cystic pancreatic lesions.

The presence of solid nodules, thick septations, and cyst wall thickening on MDCT images favors the diagnosis of an aggressive cystic lesion [2, 15, 16, 22, 30, 31]. Sahani and colleagues [15] reported that pancreatic protocol MDCT had sensitivities of 93.6%, 71.4%, and 86.4% for detecting morphologic features such as septa, mural nodules, and main pancreatic duct communication. Kim et al. [34] found that shape and wall thickness (> 1 mm) were two independent predictors of malignancy of a macrocystic pancreatic lesion. Tomimaru et al. [35] reported that the presence or absence of mural nodules on CT images had a sensitivity, specificity, and accuracy of 93%, 80%, and 86% in the diagnosis of malignant IPMNs. Sainani and colleagues [16] reported that in the detection of small cystic pancreatic lesions (≤ 3 cm), MDCT had 73.9% sensitivity for the assessment of septa and 86% sensitivity for depiction of ductal communication.

MDCT has the additional advantage of depicting calcifications, which can be difficult to recognize on MR images. Despite its improved performance in the assessment of the biologic characteristics of pancreatic cysts, false-negative results can occur because the dysplastic changes in the cystic lesions do not have distinct MDCT features [15]. In addition, MDCT has limited utility for differentiating minimally invasive carcinoma from carcinoma in situ. Similarly, the recognition of internal details and pancreatic duct communication in a small cystic lesion can be challenging with MDCT. Sainani et al. [16] reported that MRI had higher sensitivity than MDCT in showing ductal communication of small cystic pancreatic lesions (100% vs 85.7%). In addition, inflammatory changes from concurrent pancreatitis can obscure the morphologic details of cystic pancreatic lesions.

**MRI and MRCP**

MRI of the pancreas with MRCP has emerged as a reliable tool for detecting and characterizing cystic pancreatic lesions. The superior soft-tissue and contrast resolution makes MRI a sensitive study for assessing the morphologic features of cystic lesions, including their communication with the main pancreatic duct [3, 16, 30, 36, 37]. Visser and colleagues [30] found that MRI had an accuracy of 85–91% in establishing the diagnosis of malignancy in cystic pancreatic lesions. Lee et al. [2] found that MRI had an accuracy of 73.2–79.2% in determining the malignancy of cystic pancreatic lesions. In particular, in small cystic lesions (≤ 3 cm), MRI facilitates confident assessment of the morphologic features of the cyst and reliably displays small cystic lesions not obvious on MDCT images [16]. Sainani et al. [16] reported that MRI had an accuracy of 78.9–81.6% for differentiating mucinous and nonmucinous subtypes of small pancreatic cystic lesions (≤ 3 cm). They also reported that MRI had a sensitivity of 91% and 100% in the assessment of septa and main pancreatic duct communication in small cystic pancreatic lesions.

The transition from 2D software to higher-quality 3D acquisition has resulted in more effective detection of connections with the main pancreatic duct compared with the 2D single-slab technique [37, 38]. Yoon et al. [38] found that compared with 2D MRCP, 3D MRCP facilitated superior evaluation of the pancreatic duct and the morphologic details of IPMNs. The 2D MRCP sequence is usually performed as a breath-hold coronal single-shot fast spin-echo sequence or HASTE sequence [37, 38]. The 3D imaging technique is a high-spatial-resolution MRCP sequence that entails either a breath-hold turbo spin-echo sequence or a respiratory-triggered fast spin-echo approach.
An additional advantage of MRI with or without MRCP is in the follow-up of young patients with cystic pancreatic lesions because MRI eliminates exposure to ionizing radiation. Although MRCP is more sensitive in displaying the details of cystic lesions, in most cases appropriately performed thin-section MDCT in combination with image processing (multiplanar reconstructions and curved reformations) can provide sufficient detail on cystic lesions to allow decision making [15, 16]. Variants in anatomy of the pancreatic ductal system can be confidently defined with both MDCT and MRCP. This capability is important in cases of ductal anatomic variants such as pancreas divisum. The presence of such an anomaly can influence the surgical approach. A main duct IPMN affecting the dorsal duct can be treated with newer surgical techniques involving dorsal pancreatectomy and sparing the ventral pancreas, thus avoiding biliary and pancreatic anastomoses [39].

Secretin-enhanced MRCP is a modified MRCP technique in which MRI is performed after stimulation of pancreatic exocrine function by IV injection of secretin [36, 37, 40]. Through stimulation of pancreatic secretion, secretin administration can improve the utility...

Fig. 3—69-year-old woman with incidentally detected cyst in pancreatic head.
A, Axial T2-weighted MR image shows 17-mm hyperintense lesion (arrow) in pancreatic head.
B, Gadolinium-enhanced T1-weighted fat-saturated MR image shows suspicious nodular enhancement (arrow) along cyst wall. Close imaging follow-up was performed.
C and D, Follow-up MR images 1 year after B show nodule (arrow) within lesion on T2-weighted image (C) that was enhancing on gadolinium-enhanced T1-weighted fat-saturated image (D). Middle pancreatectomy was performed because of enlarging enhancing component in cyst. Histopathologic finding was side-branch intraductal papillary mucinous neoplasm with low- to moderate-grade dysplasia. Operative decision was based on development of suspicious features on follow-up images. Case falls into category of cyst with solid component.

Fig. 4—61-year-old woman undergoing follow-up of side-branch intraductal papillary mucinous neoplasm in pancreas.
A, Axial T2-weighted MR image shows 12-mm T2 hyperintense lesion (arrow) in pancreatic neck that had communication with pancreatic duct on MRCP images (not shown). No enhancing solid components or main ductal dilatation was seen. Yearly surveillance with MRI was prescribed.
B, Axial T2-weighted MR image 1 year after A shows stability of lesion size (arrow) and no development of suspicious features.
C, Axial T2-weighted MR image 2 years after A shows stability of side-branch intraductal papillary mucinous neoplasm (arrow). T2 hyperintense simple cyst in left kidney is incidental finding.
<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Pseudocyst</th>
<th>Serous Cystadenoma</th>
<th>Mucinous Cystic Neoplasm</th>
<th>Intraductal Papillary Mucinous Neoplasm Side Branch</th>
<th>Intraductal Papillary Mucinous Neoplasm Main Duct</th>
<th>Solid Pseudopapillary Neoplasm</th>
<th>Solid Pseudopapillary Neoplasma</th>
<th>Cystic Pancreatic Neuroendocrine Neoplasm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Sex</td>
<td>M &gt; F</td>
<td>F &gt; M (75%/25%)</td>
<td>F*</td>
<td>M &gt; F (60%/40%)</td>
<td>M &gt; F (60%/40%)</td>
<td>F*</td>
<td>F*</td>
<td>F = M</td>
</tr>
<tr>
<td>Location</td>
<td>Head, body, tail</td>
<td>Head, body, tail</td>
<td>Body, tail</td>
<td>Head, body, tail</td>
<td>Head, body, tail</td>
<td>Body, tail</td>
<td>Body, tail</td>
<td></td>
</tr>
<tr>
<td>Shape</td>
<td>Variable</td>
<td>Lobulated</td>
<td>Oval</td>
<td>Oval</td>
<td>Oval</td>
<td>Oval</td>
<td>Oval</td>
<td></td>
</tr>
<tr>
<td>Wall</td>
<td>Present (usually thin, thick if infected)</td>
<td>Present (thin)</td>
<td>Present (usually thick)</td>
<td>Present</td>
<td>Present</td>
<td>Absent</td>
<td>Present</td>
<td>Present (thick)</td>
</tr>
<tr>
<td>Location</td>
<td>Unilocular/ multilocular</td>
<td>Microcystic (&gt; 6, each &lt; 2 cm)</td>
<td>Macrocystic (&lt; 6, each &gt; 2 cm)</td>
<td>Macrocystic</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
<td>NA</td>
</tr>
<tr>
<td>Central scar</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>Calcifications</td>
<td>Uncommon (rim)</td>
<td>Present (20–30%)</td>
<td>Present (peripheral)</td>
<td>Present in mixed intraductal papillary mucinous neoplasms and large lesions</td>
<td>Present in mixed intraductal papillary mucinous neoplasms and large lesions</td>
<td>Present in mixed intraductal papillary mucinous neoplasms and large lesions</td>
<td>Present in mixed intraductal papillary mucinous neoplasms and large lesions</td>
<td></td>
</tr>
<tr>
<td>Main pancreatic duct communication</td>
<td>Uncommon</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
<td>Absent</td>
</tr>
<tr>
<td>Imaging predictors of malignancy</td>
<td>None</td>
<td>Typically benign</td>
<td>Solid areas and irregular wall; peripheral calcification</td>
<td>Size &gt; 3 cm; main duct dilatation (&gt; 6 mm); thick irregular wall, septa, mural nodules</td>
<td>Main pancreatic duct &gt; 10 mm; nODULES present</td>
<td>Large size, local invasion or enlarged nodes (all have very low malignant potential)</td>
<td>No specific imaging features</td>
<td></td>
</tr>
</tbody>
</table>

Note—Data from [14, 18–20, 24, 25, 27, 60, 69, 70]. NA = not applicable.

* Mucinous cystic neoplasms occur almost exclusively in women [19].

* More than 90% of patients with solid pseudopapillary neoplasm are women [25].

* All solid pseudopapillary neoplasms have very low malignant potential.

Endoscopic Ultrasound

Endoscopic ultrasound is an excellent imaging technique for detecting signs predictive of malignancy or aggressiveness in cystic pancreatic lesions. Such signs include intraductal papillary neoplasms, mural nodules, solid masses, and biliary invasion and metastasis, which can also be seen with PET/CT. Therefore, there are not enough data to justify a role of PET/CT in the characterization of cystic pancreatic lesions [27].

PET and PET/CT

PET and PET/CT have a potential advantage in detecting pancreatic neoplasms [36, 37, 40]. However, the clinical benefit of secretin MRCP in the care of pancreatic lesions [36, 37, 40] is currently unknown.
TABLE 2: Management of Commonly Encountered Cystic Lesions of the Pancreas

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Malignant Potential</th>
<th>Recommendation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudocyst</td>
<td>None</td>
<td>Referral to gastroenterologist or pancreatic surgeon if lesion is symptomatic</td>
</tr>
<tr>
<td>Serous cystadenoma</td>
<td>Very low</td>
<td>Serial imaging annually for 3 y; referral to surgeon if lesions is symptomatic or larger than 4 cm; for patients at poor surgical risk, endoscopic ultrasound (fine-needle aspiration to confirm diagnosis and rule out malignancy)</td>
</tr>
<tr>
<td>Mucinous cystic neoplasm</td>
<td>6–36% prevalence of invasive carcinoma [19] (malignant lesion is termed mucinous cystadenocarcinoma)</td>
<td>Resection if patient’s condition allows surgery</td>
</tr>
<tr>
<td>Side-branch intraductal papillary mucinous neoplasm</td>
<td>6–46% risk of development of high-grade dysplasia or malignancy [18]</td>
<td>Resection if patient’s condition allows surgery</td>
</tr>
<tr>
<td>Main-duct intraductal papillary mucinous neoplasm</td>
<td>57–92% risk of development of high-grade dysplasia or malignancy within 5 y; follow-up typically not conducted because the prevalence of carcinoma and carcinoma in situ at diagnosis is high [18]</td>
<td>Resection if patient’s condition allows surgery</td>
</tr>
<tr>
<td>Solid pseudopapillary neoplasm</td>
<td>Low malignant potential [25]</td>
<td>Resection if patient’s condition allows surgery</td>
</tr>
<tr>
<td>Cystic pancreatic neuroendocrine neoplasm</td>
<td>Variable malignant potential [25]</td>
<td>Resection if patient’s condition allows surgery</td>
</tr>
</tbody>
</table>

*Follow-up guidelines are based on Sendai criteria [22].

90.5%, 86.2%, and 88% for differentiating cystic from solid pancreatic lesions. Kim and colleagues also found that the sensitivity of endoscopic ultrasound for characterization of septa (77.8%), mural nodules (58.3%), main pancreatic duct dilatation (85.7%), and main pancreatic duct communication (88.9%) was comparable to that of MRI. However, endoscopic ultrasound is invasive and operator dependent, and these limitations have led to considerable variability in determining accuracy in differentiating benign and malignant lesions [48, 52–54]. Ahmad et al. [55] found only fair agreement (κ = 0.24) between experienced endoscopists in the diagnosis of neoplastic versus nonneoplastic cystic pancreatic lesions. In addition, several investigators have noted difficulty in sampling lesions smaller than 3 cm [48, 52–54]. Currently, endoscopic ultrasound with or without aspiration is used in the following instances: indeterminate MDCT or MRCP findings; care of patients at high surgical risk owing to co-morbid conditions or advanced age, which precludes them from undergoing extensive surgery; and confirmation of the malignant status of a cystic lesion before it is resected [48, 52–54].

Endoscopic ultrasound–guided cyst fluid aspiration is often performed in conjunction with endoscopic ultrasound for definitive diagnosis (Table 3). In a multicenter trial that included 341 patients with cystic pancreatic lesions [56], endoscopic ultrasound had low sensitivity (56%) and specificity (45%) for differentiation of mucinous and nonmucinous pancreatic cystic lesions on the basis of endoscopic ultrasound morphologic features. However, based on results of cytologic (fine needle aspiration [FNA]) evaluation, sensitivity, specificity, and accuracy were 34.5%, 83%, and 51%. Biochemical analysis of the cyst fluid aspirate for estimation of carcinoembryonic antigen (CEA), mucin, and amylase concentrations can facilitate reliable differentiation of mucinous and nonmucinous cystic neoplasms [18–20, 25, 56]. A cutoff CEA concentration of 192 ng/mL has been found to have 84% specificity in differentiation of mucinous from nonmucinous lesions [54, 56–59]. Cyst fluid amylase concentration also is helpful in differentiating pseudocysts from lesions that are not pseudocysts [56, 58, 59]. Although amylase concentrations less than 250 U/L are helpful for excluding pseudocysts, concentrations greater than 250 U/L are nonspecific because they occur not only in pseudocysts but also in benign IPMNs and MCNs [58]. FNA cytologic evaluation of the cyst fluid is also performed for cyst characterization, but the yield of cytologic evaluation is often limited by low cellularity of the fluid aspirate [18–20].

**Evidence-Based Management Guidelines**

**Imaging Appearance**

Optimal management of cystic pancreatic lesions begins with morphologic classification into one of four types: unilocular, microcystic, macrocystic, and cysts with solid components [27]. Unilocular cysts are thin-walled simple cystic lesions without internal septa, solid components, or calcifications [24, 27]. Pseudocysts are the most common lesion in this category, and usually, features of pancreatitis, such as inflammation, atrophy, and pancreatic parenchymal calcifications, are also seen [24, 27]. In rare instances, IPMNs, SCAs (< 10%), MCNs, and lymphoepithelial cysts present as unilocular cysts [27, 60].

Microcystic lesions typically present with multiple tiny cysts (more than six, each measuring < 2 cm) with lobulated outlines and thick or fleshy stroma [20, 27, 60, 61]. The microcystic appearance is typically seen in SCAs, and the pathognomonic fibrous central scar is present in only 30% of cases [20, 27, 60, 61]. Microcystic lesions can have avid enhancement on arterial phase images after
IV contrast injection owing to the presence of a vascular epithelial lining. This effect is especially pronounced in lesions with a very small cyst size, causing them to masquerade as solid pancreatic neoplasms such as neuroendocrine tumors and metastatic lesions from a primary cancer such as renal cell carcinoma or melanoma [60]. Delayed phase contrast-enhanced images can show the microcysts and the enhancing stroma. Similarly, T2-weighted MR images can confirm the presence of high-signal-intensity microcysts [20, 60]. Most SCAs have a microcystic appearance on images. Oligocystic and macrocystic patterns of SCA have been described in fewer than 10% of patients, and they can be difficult to differentiate from mucinous neoplasms on imaging [20, 61, 62].

Macrocytic lesions are composed of fewer cysts than are microcystic lesions, and the cysts are often larger than 2 cm in diameter [18, 19, 27]. MCNs and side-branch IPMNs are included in this category. Patient demographics (age, sex) and presence or absence of cyst communication can be used to differentiate MCNs and side-branch IPMNs [18, 19, 27]. MCNs are common among middle-aged women, are usually well defined, and are often located in the pancreatic tail [18, 19, 24, 27]. Side-branch IPMNs are commonly detected in older men and are more frequently located in the proximal pancreas (head and uncinate process) [18, 19, 24, 27]. An important differentiating feature between MCN and IPMN is visualization of pancreatic ductal communication. If a clear channel of communication with the pancreatic duct is visualized, the diagnosis of side-branch IPMN is almost certain because SCAs and MCNs do not communicate with the pancreatic ductal system [16, 26].

Cysts with solid components include true cystic tumors (MCNs, IPMNs) and solid pancreatic neoplasms associated with a cystic component, which includes tumors such as pancreatic neuroendocrine neoplasm, solid pseudopapillary neoplasm, adenosquamous carcinoma of the pancreas, and metastatic lesions [27]. Both MDCT and MRI can depict the presence of enhancing solid components in a cystic lesion, which is diagnostic for this category of lesions. The lesions encountered in this category are either frankly malignant or have high malignant potential. Therefore, surgical resection is the preferred management [27, 63].

Management Guidelines

With MDCT and MRI, a selective management approach can be considered for each patient after factors such as clinical presentation, age, sex, and surgical risk are accounted for [12, 22, 63, 64] (Figs. 5 and 6). The eventual management paradigm should weigh the risk of aggressiveness and the benefit of pancreatic resection. It should also include risk of development of advanced dysplastic or invasive changes in presumed mucinous lesions [12, 22, 63]. Surgery is often recommended for symptomatic cystic lesions, cystic lesions having complex morphologic features (e.g., solid components), and cystic lesions detected in patients younger than 50 years [12, 22, 63]. Asymptomatic SCAs larger than 4 cm often are resected because of a high likelihood of rapid growth and a propensity to development of symptoms [65, 66]. Because mucinous lesions have a higher propensity toward aggressive biologic behavior at detection and toward later transformation, knowledge of the mucinous nature of cystic lesions influences management [22, 31, 67, 68]. In selected patients, endoscopic ultrasound–guided cyst aspiration and FNA can be considered if the imaging findings are indeterminate or the risk of surgery outweighs the benefits.

Because MCNs are encountered in young patients and are premalignant or malignant, they are usually surgically treated at diagnosis [22]. The imaging predictors of malignancy in MCNs include large size (> 4 cm) and the presence of mural nodules and eggshell calcification [22]. Because the natural history of MCNs can follow a stepwise progression to malignancy, these lesions typically require a more aggressive approach, even when obvious imaging evidence of malignant behavior is lacking at the initial presentation [15, 22].

The prevalence of biologic aggressiveness of cystic lesions varies from 44.6% to 60% [6, 15, 30]. Biologically aggressive cystic lesions include those with overtly malignant features and lesions with higher likelihood of becoming malignant (histopathologic finding of moderate- to high-grade dysplasia) [10, 68, 69]. The prevalence of potential malignancy is higher in mucinous than in nonmucinous lesions [15, 31, 67, 68]. Mucinous cystic lesions with low-grade dysplastic changes (adenomas) are generally considered benign, and the risk of malignant transformation is unknown. Therefore, aggressive monitoring after surgical resection is not necessary [70–73].

On the basis of involvement of the pancreatic duct, IPMNs are classified as either main duct IPMN, side-branch IPMN, or mixed variant IPMN involving both the main pancreatic duct and side branches [14, 18, 22, 27]. IPMNs have distinct histologic subtypes: gastric, intestinal, pancreatobiliary, and oncocytic [74]. Main duct IPMNs often have intestinal-type epithelium, and side-branch IPMNs usually have gastric-type epithelium [74]. Although all morphologic variants of IPMN can progress to cancer, invasive adenocarcinoma originating in gastric-type IPMNs is associated with a significantly worse survival rate than that originating from other types of IPMNs [74]. However, the imaging features are not specific for differentiating the various histologic

### Table 3: Fluid Characteristics of Pancreatic Cystic Lesions

<table>
<thead>
<tr>
<th>Characteristic</th>
<th>Pseudocyst</th>
<th>Serous Cystadenoma</th>
<th>Mucinous Cystic Neoplasm</th>
<th>Intraductal Papillary Mucinous Neoplasm</th>
<th>Solid Pseudopapillary Neoplasm</th>
</tr>
</thead>
<tbody>
<tr>
<td>Nature</td>
<td>Turbid, hemorrhagic</td>
<td>Thin and clear, possibly bloody</td>
<td>Thick and viscous</td>
<td>Thick and viscous</td>
<td>Possibly bloody</td>
</tr>
<tr>
<td>Viscosity</td>
<td>Low</td>
<td>Low</td>
<td>High</td>
<td>High</td>
<td>NA</td>
</tr>
<tr>
<td>Mucin content</td>
<td>Low</td>
<td>Low</td>
<td>High</td>
<td>High</td>
<td>NA</td>
</tr>
<tr>
<td>Carcinembryonic antigen</td>
<td>&lt; 5 ng/mL</td>
<td>&lt; 5 ng/mL</td>
<td>High (&gt; 192 ng/mL)</td>
<td>High (&gt; 192 ng/mL)</td>
<td>NA</td>
</tr>
<tr>
<td>concentration</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>NA</td>
</tr>
<tr>
<td>Amylase concentration</td>
<td>High (&gt; 250 U/L)</td>
<td>Low (&lt; 250 U/L)</td>
<td>Variable&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Variable&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Low</td>
</tr>
<tr>
<td>Glycogen content</td>
<td>None</td>
<td>Abundant</td>
<td>None</td>
<td>None</td>
<td>None</td>
</tr>
</tbody>
</table>

Note—Data from [20, 24, 58]. NA = not applicable.

<sup>a</sup>High concentration of amylase (> 250 U/L) can be seen in benign intraductal papillary mucinous neoplasms and benign mucinous neoplasms.
variants of IPMNs. IPMNs can be managed either surgically or conservatively, depending on their characteristics, the clinical presentation, and the patient’s age. Because of the higher risk of invasive cancer associated with main duct lesions, resection is recommended for all main duct and mixed variant IPMNs [14, 22, 75]. In patients whose condition is considered acceptable for surgery, the type of surgical resection is influenced by lesion location and the extent of tumor foci in the duct epithelium. For side-branch IPMNs, a surgical approach is undertaken if the patient has symptoms (pain, nausea, diarrhea, weight loss, jaundice), if there is main duct involvement or dilatation (> 6-mm), if the cyst is larger than 3 cm, or complex features such as a thick irregular wall, thick septa, and solid nodules are identified on imaging [22].

Because side-branch IPMNs without complex morphologic features usually have low malignant potential, surgical management is not always warranted [4, 22]. Although the incidence of potential malignancy is lower for smaller lesions (< 3 cm), the presence of suspicious features on images, even in a small cystic lesion, should be approached more aggressively [8, 16]. Therefore, despite the low incidence of aggressiveness of mucinous cystic lesions 3 cm and smaller, the incidence is not low enough to dismiss the lesions entirely, and careful review of the imaging features is mandated. In addition, patients whose condition is found not suitable for surgical management often need frequent assessments for growth and change in imaging features [14, 15, 22].

A panel of experts have proposed the Sendai criteria as guidelines for the management of side-branch IPMN [22]. The follow-up guideline varies in accordance with the size of side-branch IPMN [22]. Lesions smaller than 1 cm are evaluated annually; those measuring 1–2 cm are evaluated every 6–12 months; and those measuring 2–3 cm are imaged at intervals of 3–6 months [22]. However, authors of more recent studies have recommended considering a longer surveillance interval of 2 years for cystic lesions smaller than 3 cm after baseline detection in the absence of mural nodules [63, 76]. Accordingly, it would be prudent to perform follow-up evaluations every 2 years for side-branch IPMNs smaller than 2 cm and to perform annual evaluations for IPMNs measuring 2–3 cm [63, 76].

The choice of imaging modality for monitoring IPMNs depends on institutional preference and the patient’s age. Although MDCT and MRI are both accepted methods for follow-up of these lesions, for adults younger than 50 years, MRI can be considered owing to concerns about radiation exposure from MDCT. Regardless of the type of imaging modality used, contrast-enhanced examinations are crucial for improving detection of enhancing solid components, the cyst wall, and septa. Contrast injection is desirable, but for patients with compromised renal function and those with lower cancer risk (small lesion, advanced age), follow-up CT or MRI can be performed without contrast injection. However, if suspicious features are observed during follow-up examinations, IV contrast medium should be used [77].

A vexing issue in the follow-up of pancreatic cystic lesions is the total duration of follow-up. It would be reasonable to increase the follow-up intervals to 2 years for lesions 2 cm and larger that are stable for 2 years. For lesions smaller than 2 cm, imaging follow-up can stop after stability has been found for 2 years. However, due consideration needs to be given to the patient’s age, symptoms, and capability of undergoing surgical resection. At follow-up imaging, lesions that are indeterminate or have a growth spurt of more than 1 cm/year, endoscopic ultrasound can be performed to confirm the malignant nature (Fig. 6). In patients in whom endoscopic ultrasound findings indicate a cystic lesion is benign, follow-up is performed in accordance with the size of the cystic lesion.

**Surgical Management**

A variety of open and laparoscopic surgical options are available for patients whose condition allows surgery. For lesions in the head of the pancreas, such as an IPMN with one or more of the aforementioned suspicious features, either a standard Whipple procedure or pylorus-sparing pancreaticoduodenectomy can be performed [5, 39, 78]. Medial segmental pancreatectomy is performed for a lesion in the neck or the body of the pancreas. For lesions involving the tail of the pancreas, the spleen is assessed for involvement because it does not necessarily have to be removed with the distal pancreas [5, 39, 78].

**Postsurgical Follow-Up**

The postsurgical follow-up of patients who have undergone resection of cystic pancreatic neoplasms depends on the histologic features. Benign MCNs do not recur and therefore require no postoperative follow-up [22]. Because the risk of local recurrence and distant metastasis is higher for malignant MCNs, postsurgical follow-up evaluations are needed every 6 months [22]. The postsurgical surviv-

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**Fig. 5**—Flowchart shows management guidelines for pancreatic cystic lesions seen on imaging. Suspicious features include presence of mural nodules, main duct dilatation, solid component, symptoms, and thick wall or septations. Differentiation of possible intraductal papillary mucinous neoplasm (IPMN) and mucinous cystic neoplasm (MCN) is based on classic imaging features. EUS = endoscopic ultrasound.
al rate for invasive IPMN varies between 35% and 60%, mortality being associated with cancer recurrence, most commonly local or extrapancreatic metastasis [79–81]. The risk of recurrence ranges from 3% to 11% [75, 79]. In cases of local recurrence, completion pancreatectomy may be necessary. It is important to emphasize that invasive IPMN has a better survival rate than pancreatic ductal adenocarcinoma [74]. Follow-up of a side-branch IPMN should be pursued carefully, and the time frame of follow-up should be based on the patient’s risk and the lesion size. Guidelines laid down by the International Association of Pancreatology call for yearly follow-up evaluations of benign IPMNs and for imaging follow-up in conjunction with measurement of serum markers (CEA and CA19-9) after resection of invasive IPMN [7, 22]. The follow-up imaging protocol used in these scenarios should consider the aggressiveness of the resected lesion and the surgical margins. Most recurrences take place within 3 years. There have been reports [69, 82], however, of recurrences that are not resected. Most incidentally identified cystic lesions can be safely followed up. Current international guidelines recommend careful cystic lesion evaluation in patients with IPMN should be performed with CT or MRI, EUS, and endoscopic ultrasound, plays an important role in risk stratification, avoiding unnecessary surgery, and safe follow-up of lesions that are not resected. Most incidentally identified cystic lesions can be safely followed up. Current international guidelines help in this regard. They are highly sensitive to identification of high-risk lesions (in situ and invasive cancer) but need further refinement to improve their positive predictive value for high-grade pathologic findings.

The Gastroenterologist’s Perspective

Cystic neoplasms of the pancreas are one of the most common indications for pancreatic surgery. Because most of the cystic lesions that we remove do not contain invasive cancer and are asymptomatic, we can state that many of these operations are preventive. Most of these lesions are IPMNs that contain only low-, moderate-, or high-grade dysplasia (what we used to refer to as in situ carcinoma), and we remove them either because we cannot reliably exclude invasive cancer or because we believe that progression will inevitably occur and the lesion will become invasive, akin to the process that occurs in a colonic polyp. The decision to operate, however, is not straightforward. Although pancreatic surgery has become safer and the risk of dying after a Whipple procedure or distal pancreatectomy is less than 2% at most major medical centers, the frequency of complications is still high (> 40%), and the consequences of endocrine and exocrine insufficiency with loss of pancreatic tissue are not trivial. These risks have to be carefully weighed against the potential benefit. Striking the right balance can be difficult because most of these lesions occur in elderly persons, and our knowledge of the natural history of IPMNs is incomplete.

Practice Recommendations

Annual imaging surveillance is generally sufficient for benign serous cystadenomas smaller than 4 cm and for asymptomatic lesions. Asymptomatic thin-walled unilocular cystic lesions smaller than 3 cm or side-branch IPMNs should be followed up with CT or MRI at 6 and 12 months interval after detection and then annually for 3 years. Cystic lesions with more complex features or with growth rates greater than 1 cm/year should be followed more closely or recommended for resection if the patient’s condition allows surgery. Symptomatic cystic lesions, neoplasms with high malignant potential, and lesions larger than 3 cm should be referred for surgical evaluation. Endoscopic ultrasound with FNA biopsy can be used preemptively to assess the risk of malignancy.

Recommendations for Further Research

Despite great strides in noninvasive imaging and endoscopic ultrasound in the characterization of pancreatic cystic lesions, current imaging techniques are not accurate in the differentiation of cystic lesions associated with carcinoma in situ or high-grade dysplasia from benign lesions. Though MDCT and MRI can reliably depict cystic lesions with obvious aggressive biologic features, their value for prediction of the biologic behavior of all the cysts is limited. Advanced techniques such as PET/MRI with targeted radioisotopes have

**Cystic Pancreatic Lesions**

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**Fig. 6**—Flowchart shows management guidelines for intraductal papillary mucinous neoplasm (IPMN). High-risk factors for surgery are old age and presence of comorbid conditions. Low-risk factors for surgery are young age and no comorbid conditions. Suspicious features are mural nodules, main duct dilatation, solid component, symptoms, and thick wall or septations. Follow-up guidelines are based on Sendai criteria [22]. EUS = endoscopic ultrasound.
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