The Incidental Pancreatic Cyst

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The discovery of a pancreatic cyst in an asymptomatic patient presents an immediate challenge to the interpreting radiologist, the clinician who manages the patient, and patients themselves. The widespread use of multidetector row CT (MDCT) or MRI in an aging population has accelerated the discovery of these lesions.

The frequency of pancreatic cysts identified with CT scanning is reported to be between 290 of 24039 (1.2%)1 and 73 of 2832 (2.6%).2 For MRI, the reported frequency is significantly higher, at between 283 of 1444 (19.9%)3 and 83 of 616 (13.5%).4 Therefore, the practicing radiologist could anticipate seeing a pancreatic cyst anywhere from 1 to 2 or 14 to 20 times per 100 cases imaged. For some practices, this could be a daily occurrence.

Although for many years the most common pancreatic cyst was believed to be a pseudocyst, cystic pancreatic neoplasms, serous cystadenoma, mucinous cystic tumor (MCT), and intraductal papillary mucinous tumors (IPMTs) now account for most of the pancreatic cysts seen in asymptomatic individuals.5 Cystic pancreatic tumors are most often benign or low-grade indolent neoplasms; however, if the cyst is mucinous (eg, intraductal papillary mucinous neoplasm or MCT), a variable but well-established malignant potential exists.6,7 This variable malignant potential of these cysts is the source of discomfort for all clinicians. The relative inaccessibility of the pancreas (as opposed to colon, breast, or even lung) to easy biopsy further exacerbates the problem.

When a cyst is discovered on an imaging study in a patient without symptoms directly referable to the pancreas, the following questions are immediately raised: can the lesion be accurately diagnosed or is the appropriate management clear from the examination, is the best management approach to suggest watchful waiting with follow-up imaging, what is the best method for imaging follow-up, and what is the optimal frequency of follow-up?

CAN THE LESION EITHER BE ACCURATELY DIAGNOSED OR IS THE APPROPRIATE MANAGEMENT CLEAR FROM THE EXAMINATION?

Morphologic features that can be assessed through imaging, allowing cyst characterization, include presence or absence of septa/loculations, presence and location of calcification, location of the mass within the pancreas, and presence of main pancreatic duct involvement8–11 (Fig. 1). Dense septa are predictive of a serous cystadenoma, although oligocystic (few or no septa) variants can be encountered.12,13 A simple but useful classification system differentiates pancreatic cysts into four gross morphologic types based solely on imaging appearance at MDCT: (1) unilocular (pseudocysts, lymphoepithelial cysts, small IPMTs), (2) microcystic (serous cystadenoma), (3) macrocystic (mucinous cystic tumor, IPMTs), and (4) cysts with a solid component (solid pseudopapillary neoplasm, mucinous cystic neoplasm).14 Overlap is anticipated in this classification, but
a likely diagnosis can be offered for most masses larger than 2 cm. Small cysts (<2 cm) will almost always appear unilocular regardless of origin.15

Serous cystadenoma is a benign lesion. Most can be described as either “honeycomb,” “sponge-like,” or oligocystic8 depending on the density of septa. Because up to 5% of them can be either unilocular or contain few septa, the term microcystic is no longer used. Calcifications are present in approximately 30% of cases and are centrally located. Lobulation is frequent. Unusual appearances can be encountered, including obstructive dilatation of the main pancreatic duct, intratumoral hemorrhage, and a solid variant.12,16

Mucinous tumors are classified into two broad categories: parenchymal and intraductal. The latter is subdivided into tumors arising in the main duct, a side branch, or a combined (mixed) form. Parenchymal mucinous lesions, referred to as MCTs, can be suspected based when a cyst is present in the tail of the pancreas. They often will have at least one recognizable septum or are unilocular. They are most frequently encountered in perimenopausal women.5 IPMTs or intraductal papillary mucinous neoplasms appear as a dilated main pancreatic duct of variable length. Branch duct IPMT will have a visible communication with the MPD. Visualization of duct communication can be defined by three-dimensional imaging either with MRI/magnetic resonance cholangiopancreatography (MRCP) or MDCT.17 They are seen more often in men.

Despite familiarity with the characteristic imaging features, many pancreatic cysts, particularly those smaller 2 cm in maximal diameter, are difficult if not impossible to specifically characterize (Fig. 2). Published studies comparing radiologic and surgical diagnosis of pancreatic cysts consistently reinforce the limitations of preoperative imaging diagnosis,15,18 creating uncertainty for radiologists confronted with one of these lesions, because some will be benign and others will be low-grade neoplasms.

**IS THE BEST MANAGEMENT APPROACH TO SUGGEST WATCHFUL WAITING WITH FOLLOW-UP IMAGING?**

Most incidental pancreatic cysts are either benign or low-grade neoplasms. Among 61 asymptomatic
patients in a cohort of 212 who had pancreatic cysts in whom operative correlation existed, 28% of asymptomatic cysts were mucinous cystic neoplasms, 27% were intraductal papillary mucinous neoplasms, 17% were serous cystadenomas, 3.8% were pseudocysts, and 2.5% were ductal adenocarcinomas. Given that only 20.8% of the asymptomatic cysts in this series were completely benign, the fact that nonoperative management is controversial is understandable. Nonetheless, ample literature supports surveillance of asymptomatic pancreatic cysts as opposed to immediate surgical resection, because they grow extremely slowly, if at all, even if they are neoplastic.

The imaging-based decision whether to resect or observe a pancreatic cyst depends predominantly on cyst size. Most studies concur that the frequency of malignancy in a cyst smaller than 3 cm is extremely low, although some recommend 2.5 cm as a maximal diameter for nonsurgical management. However, a significant percentage of these lesions smaller than 3 cm will be mucinous, but rarely is invasive cancer found in these lesions on resection. Studies of patients in whom cysts have been resected or aspirated have found that malignancy or premalignancy does not correlate with cyst size alone; these studies consider mucinous lesions of any size to be premalignant.

A retrospective case series reviewed 79 patients who underwent long-term follow-up, either for 5 years with imaging (n = 22) or 8 years with clinical follow-up (n = 27), who were diagnosed with small (<2 cm) simple pancreatic cysts on sonography or CT from 1985 to 1996. Of the 22 patients who underwent radiologic follow-up, 13 (59%) had cysts that remained unchanged or became smaller (mean size, 8 mm; mean follow-up, 9 years) and 9 (41%) had cysts that enlarged, from a mean of 14 mm to a mean of 26 mm (mean follow-up, 8 years). Of the 27 patients who underwent clinical or questionnaire follow-up (mean follow-up, 10 years), none developed symptomatic pancreatic disease. Eighteen patients (23%) died within 8 years without adequate radiologic follow-up, although none of pancreas-related causes. This experience would support the surveillance of cysts smaller 3 cm regardless of origin.

Size alone cannot be an independent decision-making variable. Radiologists must attempt to exclude the presence of morphologic abnormalities that raise the specter of a complex cyst. Aside from cyst size, other factors such as the presence of mural nodules or septations also influence the decision to resect or observe.
from a cyst larger than 3 cm, features that are worrisome include the presence of mural nodules, dilatation of the common bile duct, dilatation of the main pancreatic duct larger than 6 mm, duct wall enhancement, and lymphadenopathy27,33–37 (Fig. 3).

When a cyst larger than 1 cm is detected, before a specific radiologic-based decision is made, a dedicated “pancreas-style” study should be performed. Because smaller cysts (closer to 1 cm) are more likely to be benign, the timing of this examination is better determined through clinical decision rather than according to a rigid algorithm. One could make a case for delaying the characterization study for several months6–12 for lesions closer to 1 cm than to 3 cm. If MDCT is used for lesion characterization, a dual-phase acquisition in both pancreatic and portal venous phases using narrow detector configuration and intravenous contrast is the appropriate protocol. Thin-section images should be available on a workstation to facilitate three-dimensional analysis (Fig. 4). Alternatively, MRI performed at 1.5T can be used. The study should include sequences that display in and out of phase T1 and T2 (preferably with fat suppression), and fat suppressed three-dimensional gadolinium-enhanced sequences in pancreatic, portal, and equilibrium phases. Additionally, respiratory triggered three-dimensional MRCP is necessary.38 Secretin administration may facilitate visualization of the cyst’s communication with the main pancreatic duct.39

Many cysts are smaller than 10 mm. In a study of 421 cysts, 144 (34%) were in this size range.40 Cysts of this size are frequently detected at MRI; they are not easily characterized through imaging.

**Fig. 4.** Follow-up of side branch IPMT. (A) MDCT study detected this lesion in a middle-aged woman seen in the emergency department in 2003 for lower abdominal pain. (B) A “pancreatic-style” MDCT performed several weeks later study provided a data set that allowed creation of the CT pancreatogram confirming the diagnosis of IPMT. Because the lesion was smaller than 2 cm, the patient elected follow-up for the lesion. (C) The patient was advised to have the lesion followed up with MRI to decrease radiation exposure. This T2-weighted image was obtained in 2010; the lesion has not changed in the past 7 years.
Recommendations for following up these cysts cannot be made based on the appearance at imaging alone.

Non-imaging-based parameters are critical in the final recommendation to follow-up, resection, or ignore. The presence or absence of patient symptoms (eg, weight loss, jaundice, diabetes, anorexia) is a critical component of these decisions. Lee and colleagues found that in asymptomatic patients with pancreatic cysts smaller than 3 cm, the incidence of occult malignancy was 3.3%, whereas 90% of patients with malignant lesions were symptomatic.

The treatment philosophy of a given institution must also be factored into the decision-making process. A meta-analysis compared initial pancreaticoduodenectomy, yearly noninvasive radiographic surveillance, yearly invasive surveillance with endoscopic ultrasound, and the do-nothing approach for all cysts larger than 2 cm in the pancreatic head. Survival was maximized if all cysts were resected; however, when measuring quality-adjusted survival, the do-nothing approach maximized quality of life in patients younger than 75 years of age who had cysts smaller than 3 cm. Once age exceeded 85 years, noninvasive surveillance dominated. Initial pancreaticoduodenectomy did not maximize quality of life in any age group or cyst size.

If the decision is made to resect a cyst smaller than 3 cm, every attempt should be made to determine a specific diagnosis. Endoscopic ultrasound with fine-needle aspiration is the most widely used technique to obtain cyst content for analysis. Cyst size is the primary determinant of successful aspiration. A carcinoembryonic antigen level in the aspirate of 192 ng/mL has a high specificity for discriminating mucinous from nonmucinous

Fig. 5. Follow-up images of oligocystic serous cystadenoma in (A) 2005, (B) 2008, and (C) 2010. The patient was 56 years old in 2005. The lesion has been stable for the entire period of observation. Because of the size, the patient underwent an endoscopic ultrasound–assisted aspiration, which confirmed glycogen-rich serous fluid. The patient was dismissed from further follow-up this year; however, she was told that if she developed any pancreatic type symptoms, she would require reevaluation with further imaging.
Fig. 6. (A) Irregular pancreatic body cyst is seen in this middle-aged man in 2006. No pancreas-related symptoms were present. The mass was somewhat irregular. Aspiration under endoscopic ultrasound was suggested; however, this procedure did not yield a diagnostic sample. Follow-up was advised. (B) Follow-up MRI in 2010. T2-weighted image clearly shows the mass to be a branch duct IPMT. The lesion has not increased in size in 4 years. Further follow-up is unnecessary if the patient remains asymptomatic.

Fig. 7. Growth of lesion. (A) T2-weighted MRI from patient with vague abdominal symptoms seen in 2007 shows a high signal mass in the pancreatic head. It has no internal septa or debris, and the remainder of the pancreas was normal. Follow-up was recommended. (B) T2-weighted MRI in same patient from 2008. The mass has grown. An aspiration under endoscopic ultrasound guidance was attempted but was nondiagnostic. The patient elected to continue follow-up. (C) T2-weighted MRI in the same patient in 2009. Growth has continued. The lesion remains otherwise unchanged with no interval development of worrisome features. Surgery was recommended, and no new attempt at aspiration was made. The mass was a pseudocyst.
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THE INCIDENTAL PANCREATIC CYST

The incidental pancreatic cyst is a disease that affects the pancreas, which is a gland located behind the stomach. The cysts are typically found during routine imaging studies, such as CT scans or MRIs, and can be either benign or malignant. The management of these cysts is important to ensure that appropriate treatment is given to those who need it, while avoiding unnecessary tests or surgeries for those who do not.

WHAT IS THE BEST FOLLOW-UP METHOD?

Assuming that a lesion meets strictly applied criteria for follow-up (<3 cm, no mural nodules, no main pancreatic duct dilatation, asymptomatic), follow-up studies are often recommended in the radiologic report. Two questions are raised: what is the frequency of follow-up, and what is the optimal method of follow-up?

The frequency of follow-up examinations is not resolved. A conservative management would be to follow up a cyst for 24 months at 6-month intervals and then yearly for a second 24 months, declaring stability after 4 years. The Sendai guidelines recommend all cysts smaller than 1 cm be followed each year, all cysts from 1 to 2 cm followed as described earlier, cysts from 2 to 3 cm be followed every 3 to 6 months, and all cysts larger than 3 cm be resected. Based on longitudinal observation of 166 cysts in 150 patients, a second approach suggests having the first follow-up occur 2 years after baseline. American College of Radiology (ACR) guidelines recommend a single follow-up in 1 year for lesions smaller than 2 cm; a follow-up of every 6 months for 2 years and then yearly for lesions 2 to 3 cm; and for lesions larger than 3 cm, resect unless they are serous cystadenoma or proven to be pseudocyst through aspiration. All of these guidelines suggest that patients must remain asymptomatic during the follow-up period (Fig. 5).

The choice of follow-up method is important. The ACR subcommittee on incidental pancreatic lesions recommends MRI as the preferred follow-up procedure based on superior contrast resolution making the detection of septa, nodules, and main pancreatic duct communication easiest to recognize and the lack of ionizing radiation (Fig. 6). Cost and resource availability must be factored into this decision. For patients older than 60 years, radiation issues may not be as compelling. Regardless of the choice of follow-up procedure, care must be taken to assure that measurements are made carefully and consistently. The lesion must be carefully measured; not only must the slice number and series appear in the report but also electronic calipers must be placed on the exact image used to determine the diameters. Currently, no consensus has defined growth. The precision of manual measurement is well-known to be inversely related to the lesion diameter. Thus, determining whether the reported growth of a small lesion is true growth or measurement error may be difficult. Considerable research is currently evaluating semiautomated lesion segmentation, which will overcome this problem.

Growth alone may not be sufficient to recommend surgery; the authors believe that cyst content should be aspirated before surgical excision is performed (Fig. 7).

Recent reports have documented ductal adenocarcinoma developing in a remote site within the pancreas from a known branch duct IPMT. This finding is not surprising in that many believe the presence of a mucinous lesion is a signal of increased risk of pancreatic neoplasm anywhere within the gland. In most of these cases, the target cyst remains unchanged. The development of these lesions is thought to reflect a field effect within the pancreas, with the cyst being a signal of a gland that is at risk for developing carcinoma. Increased numbers of pancreatic intraepithelial neoplasia lesions, believed to be precursor lesions for development of ductal adenocarcinoma, are

Box 1

Recommendations for radiologists confronted with an incidental pancreatic cyst

1. Surgery should be considered for patients with cysts larger than 3 cm.
2. If the lesion is a serous cystadenoma, surgery is deferred until the cyst is larger than 4 cm.
3. Patients with simple cysts smaller than 3 cm can be followed up, but attempts should be made to characterize cysts larger than 2 cm at detection; if this cannot be done based on the available imaging study, MRI is the preferred procedure.
4. Cysts smaller than 1 cm cannot be further characterized by imaging, but can be followed up less frequently than cysts larger than 3 cm; in elderly patients (>80 years of age), these cysts likely will not require further investigation.
5. Aspiration is strongly advised to exclude pseudocyst before any surgery is performed.
6. Patients must remain asymptomatic during the follow-up period.

Fig. 8. Flow chart for imaging workup of incidental pancreatic masses in asymptomatic patients. As with all guidelines, these are not meant to be a rigid set of rules, but rather a starting point for clinically relevant decision making. BD-IPMN, branch duct intraductal papillary mucinous neoplasm; US, ultrasound. \(^a\) Signs and symptoms include hyperamylasemia, recent onset diabetes, severe epigastric pain, weight loss, steatorrhea, or jaundice. \(^b\) Consider decreasing interval if younger, omitting with limited life expectancy. Recommend limited T2-weighted MRI for routine follow-ups. \(^c\) Recommend pancreas-dedicated MRI with MRCP. \(^d\) If no growth after 2 years, follow yearly. If growth or suspicious features develop, consider resection. (From Berland LL, Silverman SG, Gore RM, et al. Managing incidental findings on abdominal CT: white paper of the ACR incidental findings committee. J Am Coll Radiol 2010;7(10):754–73.)
seen in resected specimens. Should a significant frequency of cancer develop elsewhere in the pancreas of patients with any type of cyst, follow-up imaging recommendations and surgical management of the cysts will be altered.

RECOMMENDATIONS FOR RADIOLOGISTS

The pancreas subcommittee of the ACR committee on incidental lesions developed the following recommendations for radiologists confronted with an incidental pancreatic cyst (a cyst seen in an asymptomatic patient (Box 1).

These are recommendations, not guidelines nor care standards. Fig. 8 provides these recommendations in flow-chart format. Individual patient characteristics must be factored into every decision. Many clinicians who read this probably know of single case examples that are contrary to the above recommendations. However, the extensive observational experience of the authors and concordant experience documented in the published literature validate the approach outlined in this article as a reasonable departure point for analyzing patients with incidental pancreatic cysts.

REFERENCES

