Cystic neoplasms of the pancreas; findings on magnetic resonance imaging with pathological, surgical, and clinical correlation

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Abstract

Pancreatic cysts are increasingly being identified by crosssectional imaging studies. Pancreatic cystic lesions comprise a spectrum of underlying pathologies ranging from benign and pre-malignant lesions to frank malignancies. Magnetic resonance imaging with cholangiopancreatography is a non-invasive imaging modality used for the characterization of cystic pancreatic lesions. This article will review the most common pancreatic cystic neoplasms and the utility of MR imaging in the characterization of these cysts.

Key words: MRI—Pancreas—Cyst—Neoplasm— Pseudocyst

Despite recent improvements, differentiation of the cystic pancreatic neoplasms by imaging techniques remains challenging. While the identification of a pancreatic cyst by the radiologist is relatively easy, accurate diagnosis of the specific type of pancreatic cyst or cystic neoplasm remains challenging because of overlapping and nonspecific imaging findings. Therefore, the differential diagnosis of pancreatic cysts must include a variety of neoplasms, particularly in the absence of antecedent factors or events that could generate a pseudocyst.

Epidemiology

The use of the term "cyst" to describe fluid-filled lesions of the pancreas is confusing. Many, perhaps most, use the term to encompass all cystic lesions, while others use a stricter definition that requires an epithelial lining. The term "pseudocyst," for example, originally referred to the fact that inflammatory fluid collections secondary to pancreatitis lacked an epithelial lining [1]. Generally, "cyst" is used in an inclusive manner, and simply refers to any pancreatic lesion consisting primarily of fluid.

An autopsy study of 300 patients reported that incidental pancreatic cysts were found in nearly half of the population, with the prevalence increasing with age. While most of these cysts were non-neoplastic, 3.4% of patients had cysts that showed epithelial atypia [2]. The prevalence of incidentally detected pancreatic cysts on MR imaging was found to be as high as 13.5% [3]. The most common pancreatic cystic neoplasms include intraductal papillary mucinous neoplasm (IPMN), mucinous cystic neoplasms (MCNs), serous cystadenoma (SCA), pseudocyst (14%), and some of the less common cystic tumors are ductal adenocarcinomas, cystic endocrine neoplasms, lymphoepithelial cysts (LECs), and solid pseudopapillary neoplasms (SPNs) [4] (Table 1). Most patients (67%) with pancreatic cystic neoplasms are asymptomatic, but for those with symptoms the most common presenting complaints are abdominal pain, followed by weight loss (38%) and pancreatitis (36%) [4].

Pathological classification and risk of malignancy

All patients with pancreatic cysts, whether asymptomatic or symptomatic, must be thoroughly investigated to ascertain the underlying nature of the cyst. When evaluated by size criteria alone, only 3.5% of asymptomatic

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Neoplasm	Incidence (%)
IPMN	37
Mucinous cystic neoplasm	21
Serous cystadenoma	12
Pseudocyst	14
Ductal adenocarcinoma	8
Others	8

cysts smaller than 2 cm have potential for developing into cancer compared with 26% of cysts larger than 2 cm [4]. Most serous lesions are benign and have little or no malignant potential, whereas approximately half of the mucinous lesions are pre-malignant [4]. In 1996, the World Health Organization (WHO) classified cystic mucin-producing pancreatic neoplasms into two distinct entities: intraductal papillary mucinous tumors and mucinous cystic tumors. In the 2000 revision of the WHO classification [5], these two neoplasms were renamed as IPMN and MCN, respectively. Since then, much has been learned regarding the clinical, radiographic, and histological characteristics of these neoplasms.

IPMNs are subdivided into main duct (either diffuse or segmental), mixed or side-branch types, depending on their location in the ductal system [6]. Side-branch IP-MNs are the most common type. Five histologic types of IPMN have been recognized: gastric foveolar type, intestinal type, pancreatobiliary type, intraductal oncocytic papillary neoplasm, and intraductal tubulopapillary neoplasm. Non-invasive IPMNs are classified into three grades based on the degree of cytoarchitectural atypia: low-, intermediate-, and high-grade dysplasia. The most important prognosticator, however, is the presence or absence of an associated invasive carcinoma. The reported risk of in situ or invasive malignancy in postsurgical patients with main duct IPMN ranges from 57% to 92% [7], and is far less in patients with side-branch IPMNs (25%) [8]. Preoperative prediction of the malignant potential of an IPMN is of growing importance because pancreatic surgery can have serious complications, and many small IPMNs, especially side-branch type, have a very low risk of progression to an invasive type. It is hoped that better understanding of the molecular genetics of IPMN may help identify molecular markers for a high-risk lesions [9]. Nonetheless, given sufficient time, even benign main duct IPMNs may progress into invasive cancer. The long-term follow-up of resected patients shows 100% survival for benign and non-invasive neoplasms, and 5-year survival rates between 36% and 60% for patients with coexistent invasive carcinomas [10].

MCNs are lined by mucin-producing epithelial cells with the most characteristic histological finding being the presence of a unique subepithelial ovarian-type stroma [11]. MCNs occur almost exclusively in women with a

mean age of about 60 years [12]. Non-invasive MCNs (mucinous cystadenomas) can be categorized into low-, moderate-, or high-grade dysplasia (carcinoma-in situ). Invasive MCNs are also referred to as mucinous cystadenocarcionomas, and these malignancies can infiltrate into adjacent organs. MCNs demonstrate significant amount of variability in mucin content and the degree of cytologic atypia of the epithelial cells lining the cyst. Due to sampling issues, fine needle aspirates of these cysts may not accurately reflect their true nature. Integration of the clinical and imaging findings of the cyst including factors such as gender, location, and communication with the main pancreatic duct (MPD) aids the cytopathologist in rendering a diagnosis from aspirates [13]. Malignant transformation from SCAs is exceedingly rare [14, 15], and therefore these tumors are considered to have a negligible malignant potential.

Incidental cysts measuring 2 cm or smaller are found to be associated with a very low lifetime risk of cancer (3.5%) [4]. However, for cystic lesions ranging in size from 2 to 3 cm, the validity of utilizing size criteria has been questioned as a sole predictor for malignancy, with the rate of growth rather than the initial size having been proposed as a more reliable predictor of malignant risk [16]. If patients with pancreatic cystic lesions are managed by size criteria alone, then up to 20% will receive inappropriate treatment [16]. Shorter follow-up intervals or empiric surgical resection were suggested for cystic lesions with more complex features or with growth rates greater than 1 cm per year [17].

MR imaging

MRI has superior sensitivity for detecting cysts compared to computerized tomography (CT) that has reasonable accuracy in characterization of cystic pancreatic lesions. However, both modalities are limited by a substantial rate of misdiagnosis even when reviewer certainty is high [18]. CT interpretation can be confounded by morphologic overlap between different cystic lesions and is insensitive in differentiating serous from mucinous neoplasms [19, 20]. Imaging features that help differentiate cystic pancreatic lesions from one another include the presence or absence of internal septa, including multiple fine septae that usually characterize SCA lesions; enhancing mural nodules; and the presence or absence of ductal communication. MRI with MRCP examination has an advantage over CT by better depicting the internal morphology of the cyst due to the superior soft tissue contrast, thereby facilitating the recognition of septae, nodules, and ductal communication [8, 21, 22]. When patients are required to undergo frequent imaging for follow-up, the enhanced clinical value of MRCP compared to CT becomes more obvious due to lack of radiation exposure associated with MRCP [8]. However, disadvantages of MRI include lower spatial

	2 point DIXON	SSFSE	SSFSE	STIR	MRCP2D slab	3D TSE with variable flip angle	MRCP 2D slab with secretin	3D GRE with contrast
Plane of acquisition TR/TE (m)	Axial 7.47/4.76 (in), 2.38 (out)	Axial 1100/90	Coronal 1100/90	Axial 2900/132 (TI 150)	Coronal 2000/755	Coronal 2500/691	Coronal 2000/756	Axial 5.17/2.52
Flip angle Slice thickness Fat saturation	10° 3.4 No	130°–50° 4.0 No	130° 4.0 No	180° 7 N/a	180° 40 Yes	Variable 1 Yes	1° 40 Yes	12° 3.0 Yes

Table 2. Example parameters for pancreatic imaging on 1.5 T MRI scanners

2D, two-dimensional; 3D, three-dimensional; STIR, short tau inversion recovery; SSFSE, single-shot fast spin echo; GRE, gradient echo

resolution, insensitivity to detect calcifications, and motion-related artifacts.

MRCP is mainly based on acquisition of heavily T2weighted images, with variants of fast spin echo (FSE) sequences. However, examination also includes typical sequences such as T1-weighted in-phase and out-of-phase images and multi-phasic contrast-enhanced series for a complete evaluation of both solid pancreatic lesions and pseudotumors (e.g., mass-like lesions with focal fatty infiltration). Examples of MRCP sequences for 1.5 Tesla are listed in Table 2 [23]. The most common indications for performing MRCP in routine clinical practice are evaluation of the pancreatic ductal anatomy, characterization and follow-up of the cystic pancreatic neoplasms before and after surgery, and evaluation of the patients with acute or chronic pancreatitis for complications.

Endoscopic evaluation and tumor markers

Endoscopic retrograde cholangiopancreatography (ERCP) has traditionally been used to collect ductal fluid for cytologic evaluation, but has very limited potential for imaging of parenchymal cysts and has a reported complication rate of 11.2% [24]. Endoscopic ultrasound (EUS) is increasingly being used for the purpose of close-up sonographic evaluation and for obtaining fine needle aspiration samples directly from the cysts. Unlike ERCP, the incidence of serious complications is low with the EUS; 2.2% according to one study [25]. Mucin, if present, is a diagnostic of mucinous lesions (either MCN or IPMN), while high glycogen fluid is found in serous neoplasms. In addition to cytologic evaluation, which can be limited by the frequent hypocellularity of aspirated fluid, analysis of tumor markers can provide a clue to a cyst's malignant potential. Molecular studies analyzing the cyst-fluid DNA revealed that K-ras, tumor proto-oncogene mutations commonly seen pancreatic adenocarcinomas, are present more often in malignant lesions compared with benign lesions [26]. However, in actual clinical practice, these tests have failed to accurately differentiate benign from malignant, or mucinous and non-mucinous cysts [27].

While there is considerable overlap between imaging characteristics of mucinous and non-mucinous cysts, it has been demonstrated that cyst-fluid CEA analysis is very useful for separating serous from mucinous cysts [28]. A cyst-fluid CEA level less than 3.1 ng/mL is highly diagnostic of SCAs, and values more than 480 ng/mL are suggestive of a mucinous lesion [29]. Early studies using percutaneous FNA reported that a CEA below 5 ng/mL provided 100% sensitivity and 86% specificity for distinguishing mucinous neoplasms from other cystic lesions [30]. A large prospective study determined that a cyst-fluid CEA cut-off of 192 ng/mL provided a sensitivity of 73% and specificity of 84% for differentiating mucinous from non-mucinous tumors [31]. Cystic fluid amylase level is usually elevated in pseudocysts and IPMN, and low in MCNs. A fluid amylase level of <250 U/L supports diagnoses of SCA, MCN, or mucinous cystadenocarcinoma (sensitivity 44%, specificity 98%), and thus virtually excludes pseudocysts from consideration [32].

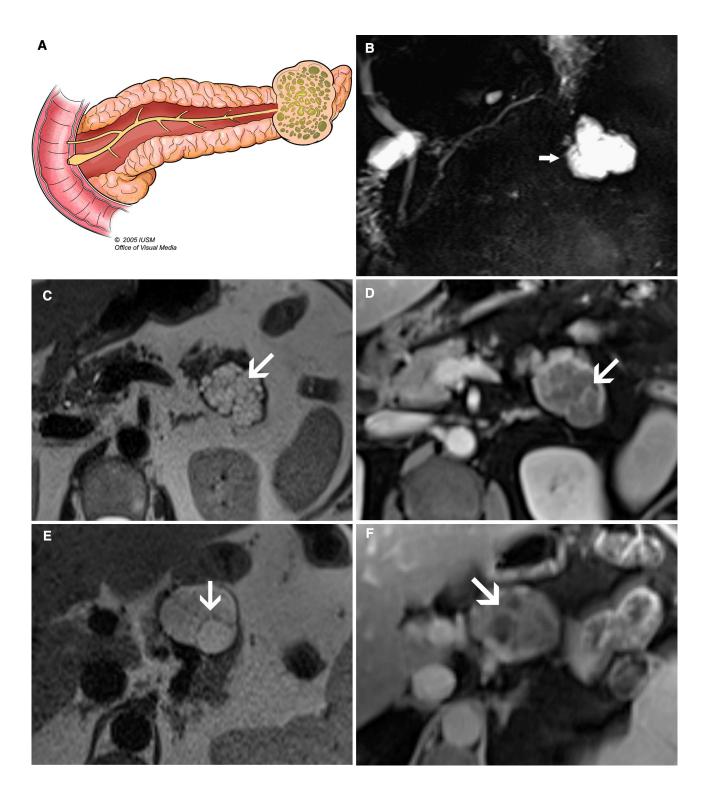
Clinical evaluation and follow-up by imaging

Currently, there are no universally accepted pre- or postoperative evaluation guidelines for patients with cystic pancreatic neoplasms. Most proposed schemes arose from a consensus conference by the working group of the International Association of Pancreatology that

Table 3. 2012 International Association of Pancreatology imaging recommendations for the management of IPMN and MCN [8]

Cyst size	Recommendation
>3 cm with worrisome features*	Surgery, if findings confirmed by EUS
2–3 cm	EUS in 3-6 months, then lengthen follow-up interval alternating MRI with EUS as appropriate.
1–2 cm	MRCP yearly for the first 2 years, then lengthen intervalif there is no change
<1 cm	CT/MRI in 2–3 years

* Worrisome features described as thickened/enhancing cyst walls, main duct size 5–9 mm, non-enhancing mural nodule, and abrupt change in caliber of pancreatic duct with distal pancreatic atrophy



addressed the management and follow-up of mucinous pancreatic cysts (IPMN and MCN). This group published their guidelines in 2006 [33] followed by a revision in 2012 [8]. At baseline, history/physical examination and MRCP (or pancreatic protocol MDCT), EUS with cytopathologic evaluation supplemented by CEA, and molecular analysis are recommended. The decision to follow a mucinous neoplasm should be made based on clinical judgment considering the patient's age, family history, symptoms, comorbidities, perceived pancreatic cancer risk, and patient preference. Table 3 lists recommended follow-up intervals for lesions based on its size and worrisome features. Recommended interval is 3– 6 months for lesions 2–3 cm, annual follow-up for lesions 1–2 cm for the first 2 years, and 2–3 year followup for lesions less than 1 cm. Cysts >3 cm and without Fig. 1. SCA. A. Illustration of the polycystic form of SCA. These represent 70% of the cases and contain multiple small cysts. SCAs are more common within the pancreatic body or tail, varying in size from 2 to 16 cm. These tumors have negligible malignant potential. They can reach very large dimensions and may cause symptoms. Published with permission. Copyright 2005, Indiana University School of Medicine Visual Media. B 64-year-old asymptomatic female patient was found to have a pancreatic cyst. Coronal S-MRCP image demonstrated a 3.2 cm \times 4.1 cm lobulated cystic mass (arrow) within the tail of the pancreas. The cyst shows no communication with the main duct. The main pancreaticduct is not dilated. C Axial T2-weighted image demonstrates the characteristic microcystic internal architecture of the polycystic form of SCA. D Axial contrast-enhanced T1-weigthed image with fat saturation shows enhancing septae (arrow). The cyst was aspirated and tumor markers were negative, and therefore final diagnosis was confirmed as SCA. Patient was asymptomatic and surgery was not performed. This lesion has remained stable in size for 5 years on follow-up by imaging. E A 53-year-old female was admitted to the hospital reportedly with staphylococcal bacteremia arising from a cellulitis. She had no prior history of pancreatitis. A CT scan found an incidental 4.1 cm \times 5.4 cm pancreatic cyst. MRCP performed for characterization, and axial T2-weighted image shows the mass within the pancreatic tail with thin internal septations (arrow). F Axial contrast-enhanced T1weighted image with fat suppression shows enhancing septations (arrow). Macrocystic variant of the SCA is less common but can be difficult to differentiate form MCN. Endoscopic aspiration was performed to exclude a mucinous neoplasm. Serum tumor markers were negative. Mass was stable on follow-up by imaging for 5 years and patient remained asymptomatic.

worrisome features can be considered for EUS to verify the absence of thickened walls or mural nodules.

Surgery is recommended for patients with secure diagnosis of MCN and main duct or mixed type IPMN. For patients with side-branch IPMNs, surgery is recommended if worrisome features of the cysts such as size > 3 cm with thickened cyst wall, MPD size 5–9 mm, non-enhancing mural nodules, abrupt change in MPD caliber with distal pancreas atrophy, and lymphadenopathy are noted. Additional "high-risk stigmata" of jaundice, enhanced solid component, and MPD > 10 mm are also the indications for resection based on the current guidelines.

The American College of Radiology has released recommendations authored by members of an Incidental Findings Committee who have recommended follow-up by MRI in 1 year for cysts smaller than 2 cm, with evaluation and close-interval follow-up by MRI/MRCP for cysts measuring 2–3 cm, and cyst aspiration or surgery to be considered for cysts greater than 3 cm [34]. All of these recommendations are affected by patient age and sex, cyst location, the presence of symptoms, and comorbidities. A recent study suggested that using MR contrast agent is not necessary for follow-up of cystic pancreatic neoplasms [35].

Follow-up of IPMN after surgery depends on multiple factors. Residual IPMN lesions or appearance of new lesions warrant continued follow-up. Some surgeons continue surveillance at short intervals owing to concern over the development of pancreatic ductal adenocarcinoma after resection of IPMN [36]. MCNs are almost always solitary, and complete resection of a non-invasive MCN does not require any post-operative surveillance [37].

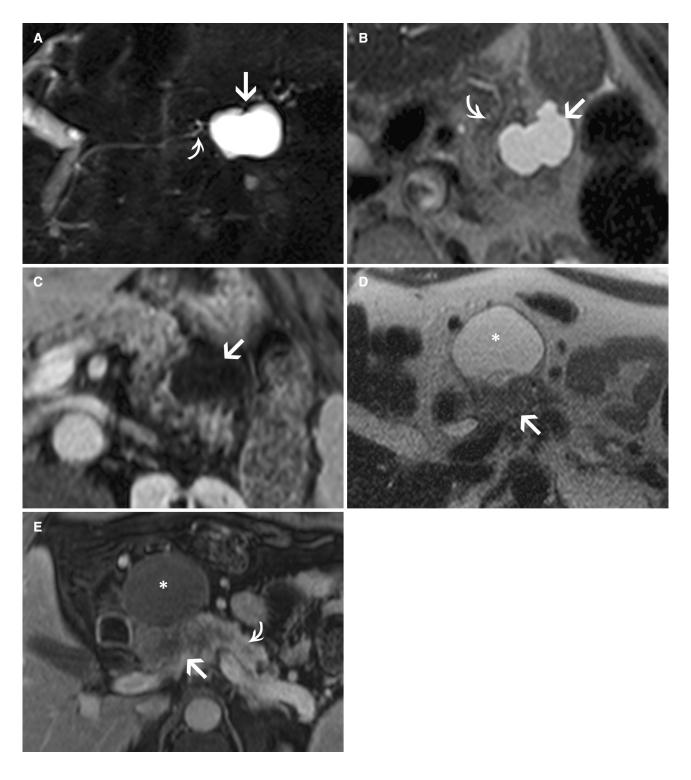
Serous cystadenoma (SCA)

SCAs are characterized by their microcystic appearance on imaging. Cysts with enhancing thin septations can be used to distinguish these tumors on T2-weighted images (Fig. 1). SCAs are more frequent in women (65%), and the mean age of diagnosis has been reported to be 62 years (range 35–84) [38]. The most common site for SCAs is the pancreatic body or tail, with the size of these cystic neoplasms varying widely from 2 to 16 cm [39]. Patients with the Von Hippel-Lindau syndrome have predisposition to develop SCAs. These lesions can grow over time and potentially reach very large dimensions, sufficient to cause symptoms usually from mass effect. Surgery may be performed to provide symptomatic relief and if the diameter of the lesion exceeds 4 cm [40], although empiric resection based on size criteria alone has been challenged [16]. In the setting of an asymptomatic cyst measuring <4 cm, a conservative approach with follow-up imaging has been recommended [40].

There are two forms of SCAs: polycystic (also termed microcystic) and oligocystic form [41]. The polycystic form, which contains multiple small cysts, represents about 70% of cases. The presence of a central calcified "stellate" scar or the characteristic "honeycombed appearance" is also diagnostic of this SCA [20] but is seen in only 30% and 20% of patients, respectively [41]. The associated microcysts contain watery, clear fluid, and can be difficult to detect by CT. On MRI studies, microcystic SCA typically presents as a lobulated cystic lesion. The oligocystic form appears as a unilocular or large multilocular cyst [42] and cannot be reliably distinguished morphologically from MCN [41].

Mucinous cystic neoplasms (MCN)

Mucinous pancreatic lesions are divided into two broad types of lesions, those that arise in the pancreatic ductal systems, which are termed intraductal papillary mucinous lesions, and those that do not, which are referred to as MCNs of the pancreas. MCNs are uncommon, and largely limited to women. Their diagnosis rests on the presence of ovarian-like stroma underlying the mucinous epithelial lining, features that can only be identified following histopathologic evaluation of the resected



neoplasm. Most mucinous pancreatic lesions are not MCNs, but are more accurately termed IPMNs using currently accepted terminology. About 75% of MCNs are located in the body or tail of the pancreas [43]. In contrast to SCAs, MCNs have considerable malignant potential, and therefore surgical management is recommended much more for patients with MCN than other

neoplasms [8, 44] particularly when worrisome imaging features, high-grade atypia, or an aggressive molecular profile (based on DNA analysis) are identified on cytologic and molecular analyses.

Morphologically, MCNs are predominantly macrocystic (80%), but can be multilocular (20%) or have several adjacent cysts [41]. These cysts can demonstrate ◄ Fig. 2. MCN. A An 84-year-old female with history of recurrent episodes of pancreatitis. Coronal MRCP image demonstrates a dominant lobulated cyst in the tail measuring 3.2 cm (arrow). The MPD is not dilated. On this coronal image, the cyst overlaps with the MPD (curved arrow). B Axial T2-weighted image shows a unilocular cyst with no visible internal septations, nodularity or debris (arrow). There is no definite communication with the MPD (curved arrow), since the duct is effaced and not visualized around the mass. C Axial contrast-enhanced T1-weighted image with fat suppression shows no internal enhancement (arrow). Tumor markers were normal within the cyst aspirate. Patient underwent elective distal pancreatectomy secondary to intermittent episodes of abdominal pain. Surgical pathology confirmed a mucinous cystadenoma. D 51-year-old female with abdominal pain, jaundice, and 30-lb weight loss was referred for evaluation of a cystic pancreatic mass. Axial T2-weighted image without fat suppression shows a large tumor within the head and neck of the pancreas with both cystic (asterisk) and solid (arrow) components. The solid part of the mass lesion was approximately 4.0×5.0 cm and the cystic component 3.8×4.0 cm in diameter. Septations are visualized at the interface of cystic and solid parts. E Axial contrast-enhanced T1-weighted image shows the infiltrating solid component of the mass (arrow). Solid part is relatively hypoenhancing to the normal pancreatic parenchyma during the venous phase. There was no enhancement within the cystic component (asterisk). The upstream pancreatic gland is atrophic, and the duct is dilated (curved arrow). These imaging findings were concerning for malignancy and biopsy confirmed mucinous cystadenocarcinoma.

thick walls and solid components. About 25% of lesions can demonstrate a peripheral eggshell calcification on CT, which is predictive for malignant nature [20]. While MRI is insensitive for detecting calcifications, it can better depict the cyst wall and internal septa [45], which leads to equally high accuracy [18] (Fig. 2). Mixed T2weighted signal intensity of the cysts may be present depending on the presence of hemorrhage. Post-contrast T1-weighted images are useful for visualization of thick septa or enhancing mural nodules, either of which may indicate potential malignancy. An important feature distinguishing MCNs from side-branch IPMNs is that they do not communicate with the MPD [41, 46]. However, this communication may not be easy to determine if the lesion abuts the duct.

Intraductal Papillary Mucinous Neoplasm (IPMN)

IPMN is the most common cystic pancreatic neoplasm. IPMNs are usually considered to be more common in men, although an equal prevalence in both sexes has been reported [47], and the mean age at the diagnosis is 65 years [10]. These tumors are characterized by intraductal proliferation of neoplastic mucinous cells forming papillary projections into the pancreatic ductal system, which is typically dilated and contains globules of mucus (Fig. 3A, B, C). Patients with IPMN can present with symptoms caused by obstruction of the pancreatic duct system or they can be asymptomatic.

Pancreatic ductal imaging is essential in establishing preoperative diagnosis and in differentiating between the different subtypes [8]. One of the most common indications of MRCP is distinguishing isolated side-branch IPMNs from other cystic lesions such as MCN or pseudocyst (Table 4). MRCP can distinguish side-branch IPMNs by demonstrating communication between the MPD and the cyst [48]. This distinction is important since observation alone may be appropriate for sidebranch IPMN lesions. Side-branch IPMNs can be managed by follow-up, as long as the cyst size is <3 cm and there is no thickened cyst wall, MPD size 5-9 mm, nonenhancing mural nodules, abrupt change in MPD caliber with distal pancreas atrophy, and lymphadenopathy [8]. Improvement in the visualization of the duct has been reported with the use of the hormone secretin [49, 50], which stimulates the pancreas to secrete significant amount of fluid, while transiently increasing the tone of the sphincter of Oddi.

The main duct IPMN involves the entire MPD or a portion of it, and manifests as abnormal ductal dilation. Radiologic features that correlate with a higher risk of malignancy include main duct type size and involvement, the presence of nodules, solid components of the tumor or wall thickening, and invasion of the adjacent structures [51]. Main duct IPMN is characterized by segmental or diffuse dilation of the MPD > 5 mm after excluding other potential causes of ductal obstruction. Main duct dilation of 5–9 mm is a worrisome feature and, a diameter of >10 mm is considered as a high-risk finding [8]. Parenchymal atrophy is often present and is related to the severity of main duct IPMN. This tumor can be difficult to distinguish from chronic pancreatitis, as both may have a similar appearance (Fig. 3D) [49].

Pseudocyst

A pseudocyst is an inflammatory fluid collection, which usually occurs as a consequence of acute pancreatitis causing a side-branch or main duct disruption. Pancreatic or peri-pancreatic necrosis will progressively liquefy in the weeks and months following an episode of acute pancreatitis. This entity is often referred to as a pseudocyst but may be better described as an organized pancreatic or peri-pancreatic fluid or necrosis collection, depending on its primary composition. The term pseudocyst is best reserved for collections that have matured to the point where a fibrous capsule, not a true epithelial lining, is present, and this process usually takes at least 4-6 weeks to develop after the onset of acute pancreatitis. Pseudocysts are cystic collections of fluid containing a high concentration of pancreatic enzymes, necrotic debris, fibrin, and blood. Pseudocysts are known to cause

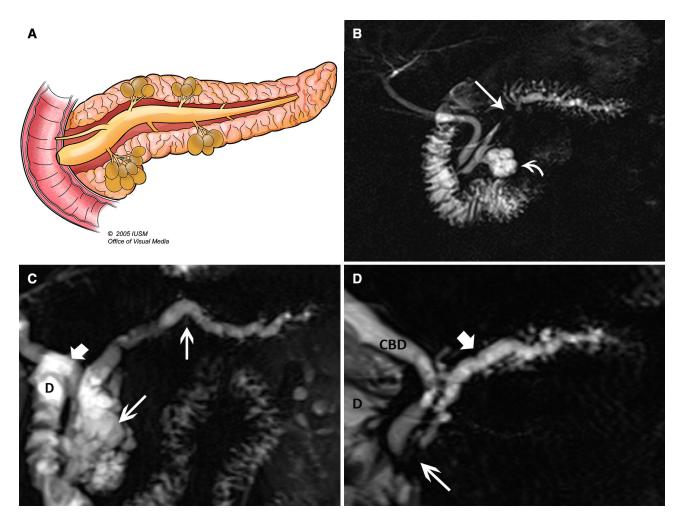


Fig. 3. IPMN. A The cysts of the side-branch IPMN are usually multiple. The diagram illustrates multifocal sidebranch IPMN, each individual lesion in turn consisting of multiple cystic lobulations. Demonstration of communication with the MPD is a very important diagnostic criterion and, when visible, can distinguish side-branch IPMNs from other cystic pancreatic neoplasms. Published with permission. Copyright 2005, Indiana University School of Medicine Visual Media, **B** A 70-year-old male with abdominal pain was referred to our hospital with diagnosis of acute pancreatitis. Coronal S-MRCP image showed a 2 cm, "grape-like" lobular cystic mass within the pancreatic head, which connects to the MPD consistent with a side-branch IPMN (curved arrow). Study also demonstrated a stricture in the neck of the pancreatic duct (arrow) causing upstream main and side-branch ductal dilatation. Patient underwent Whipple procedure for IPMN. The stricture was found to be benign. C A 73-year-old

serious complications such as perforation, abscess formation, compression of adjacent organs (e.g., stomach or duodenum), and hemorrhage. Uncomplicated pseudocysts generally show high signal on T2-weighted images, but may have mixed signal characteristics depending on female patient with a history of abdominal pain and weight loss. Coronal MRCP image shows abnormal dilatation of the entire MPD (long arrows). The ductal dilatation is more prominent, even globular in the pancreatic head, and was considered suspicious for an intraductal tumor. ERCP was performed and aspiration of the pancreatic fluid consisting of abundant mucin confirmed the diagnosis of IPMN. (Short arrow common bile duct; D, duodenum.) D 45-year-old patient with known history of idiopathic chronic pancreatitis. Coronal MRCP image shows diffuse dilatation of the MPD including the side-branches (short arrow). MPD measures up to 6 mm, and appearance is similar to the mixed type IPMN seen on Fig. 3C. Reason for this dilatation in this case was suspected to be a stricture/stone within the downstream duct (long arrow). ERCP was performed to confirm these findings. Common bile duct (CBD) was also dilated. (D, duodenum).

fluid content. The presence of necrotic debris is suggested to be highly predictive of a pseudocyst [52] (Fig. 4). There can be internal septations in both the pseudocysts and cystic pancreatic neoplasms. Microlobulated morphology favors SCA [53], while most pseudocysts show

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Characteristic	MCN	IPMN
Gender predilection	Female (95%)	Male (70%)
Age (decades)	4th and 5th	6th and 7th
Location (body and tail)	95%	30%
Shape	Rounded	Lobulated
Pancreatic duct communication	Infrequent	Yes (although not always demonstrated)
Main pancreatic duct	Normal or deviated	Normal or dilated (mixed type IPMN)

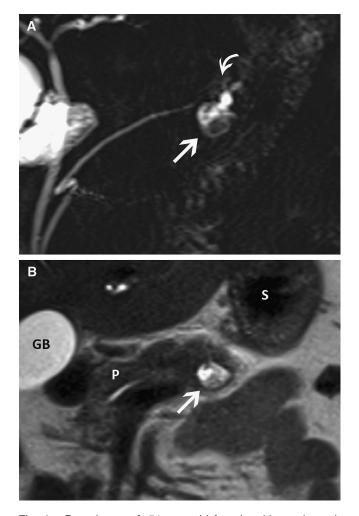


Fig. 4. Pseudocyst. **A** 51-year-old female with a prior episode of pancreatitis. Coronal MRCP image showed a 3.1 cm \times 2.9 cm cyst (*arrow*) within the pancreatic tail. There is a tiny channel of communication (*curved arrow*) between the cyst and MPD which is a finding commonly seen with the side-branch IPMN. An important finding is that the cyst does not show a homogenous T2-weighted signal. **B** Coronal T2-weighted image confirms inhomogeneous T2-weighted signal and post-contrast image (not shown) showed no internal enhancement. These findings favor a pseudocyst containing debris. Serum tumor markers were negative. (GB, gallbladder; P, pancreas; S, stomach).

round or oval morphology [54]. The presence of parenchymal atrophy, dilation of the pancreatic duct, and most importantly a history of acute pancreatitis favors the diagnosis of a pseudocyst [55].

Other lesions

SPN of the pancreas

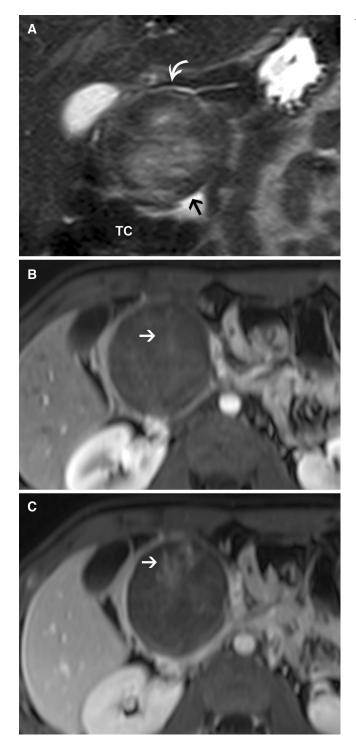
SPN of the pancreas is found within the pancreas and almost exclusively seen in young women (average age 25). These tumors usually present as a large and encapsulated mass and have low-grade malignant potential [56]. The solid and cystic components result in heterogeneous T2weighted signal in majority of patients [57]. The cystic components are not "true" cysts, as they lack an epithelial lining, but rather represent a necrotic/degenerative process containing blood and debris [58]. Increased T1-weighted signal can be seen secondary to hemorrhage. Solid parts of the tumor show mildly increased T2-weighted signal compared to the pancreas. These tumors demonstrate progressive enhancement on multi-phasic contrast-enhanced series (Fig. 5). SPNs generally displace the surrounding structures rather than invading them. Because of their soft consistency, SPNs rarely cause biliary or pancreatic ductal obstruction, even when located in the head of the pancreas [57]. Metastasis is rare, and surgical resection is curative in the majority of patients [58].

Cystic neuroendocrine neoplasms of the pancreas

Pancreatic neuroendocrine tumors (PanNETs) are usually well-vascularized solid lesions and majority are non-functional [59]. Cystic PanNETs were thought to be very rare; however, according to a recent, large study, this variant accounted for in 17% of 170 PanNETs [60]. Cystic neuroendocrine neoplasms are larger in size and more likely to be symptomatic at presentation but are less likely to be functional compared to the solid counterparts [60]. Two thirds of these tumors are partially cystic, and the cysts are typically filled with serosanginous fluid [58]. There are no specific radiologic findings to differentiate them from other pancreatic cysts (Fig. 6). Correlation of imaging findings with the clinical history is advised to include this neoplasm in the differential diagnosis. Patients with a cystic PanNET are 3.5 times more likely to have an underlying multiple endocrine neoplasia syndrome (MEN type 1) than patients with a uniformly solid neuroendocrine tumor [60].

Lymphoepithelial cysts

LEC of the pancreas is a rare lesion that may mimic a SCA, pseudocyst, or MCN. Most of these tumors are



asymptomatic and are discovered as incidental findings by imaging studies. They are seen predominantly in adult men (mean age 56, range 35–74 years; M/F: 4/1) and may occur anywhere within the pancreas (head, body, or tail). LECs can be multilocular (60%) or unilocular (40%), and are lined by squamous epithelium [61]. MR

Fig. 5. SPN of the pancreas. A 15-year-old female presented with abdominal pain. Coronal T2-weighted image shows a 5.7 cm mass located in the pancreatic head, causing mass effect to the transverse colon and gallbladder. There is heterogeneous T2-weighted signal with some areas showing increased signal suggestive of cystic change. The pancreatic duct is not dilated but displaced superiorly by the mass (*curved arrow*). There is no evidence of invasion of the surrounding organs. T2 hypointense capsule (*arrow*) is visible. There was no dilatation of the common bile duct (not shown). B Axial T1-weighted image following contrast injection obtained at early phase shows mild degree of internal enhancement (*arrow*). C Axial T1-weighted image acquired after 2 min of delay of contrast injection shows progressive enhancement (*arrow*).

imaging findings of LECs have not been described in the literature (Fig. 7). A recent case report described profound restricted diffusion due to the presence of keratinized material found within the LECs [62]. Another case series involving eight patients evaluated these cysts by CT. Approximately, 75% of LECs showed an extrapancreatic location with an average size of 3.4 cm. Morphologic features were similar to that of SCAs and pseudocysts. There were no enhancing nodules [63].

Surgical approach to non-inflammatory pancreatic cysts

From a surgeon's clinical perspective, the fundamental question related to pancreatic cysts is does the cyst need to be removed? Indications for surgery include symptoms, a clinical concern for malignancy, and interval growth. A cyst growth over serial imaging is a common indication for operative resection.

A careful clinical history will elicit common symptoms. Pain is common, and may be clearly related to cyst location (i.e., pancreatic tail cysts often cause left-sided pain that radiates to the left shoulder). Gastric outlet obstruction may cause potentially subtle symptoms such as nausea, early satiety, or increased gastroesophageal reflux. Radiologic imaging compliments clinical evaluation. Gastrointestinal luminal impingement (either gastric or duodenal) is easily seen on cross-sectional imaging. Similarly, biliary obstruction by cysts in the pancreatic head or uncinate process may actually be anticipated radiologically before any noticeable clinical manifestation such as elevation of circulating liver chemistry tests or jaundice. Patients with mucinous cysts (especially IPMN) may have secondary mild acute pancreatitis caused by the cyst manifested by pancreatic edema and peri-pancreatic fat stranding on cross-sectional imaging.

MRI is not only important for diagnosis, but also for surgical planning: enucleation vs. resection (and type of

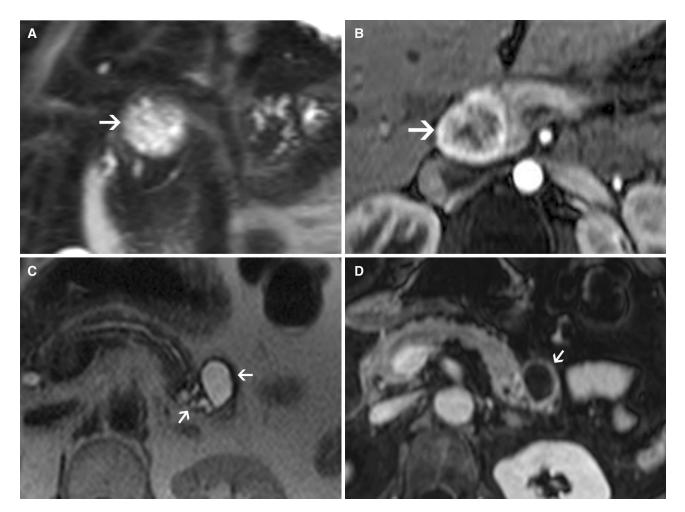
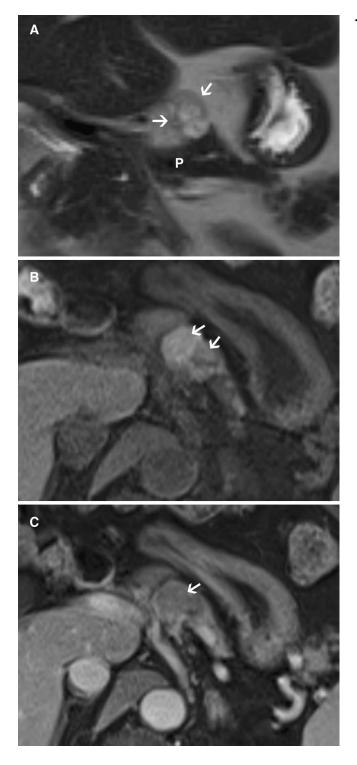


Fig. 6. Cystic PanNET. **A** A 42-year-old female was found to have a pancreatic cyst. Coronal T2-weighted image shows a round inhomogeneous T2 hyperintense mass (*arrow*) within the superior aspect of head of the pancreas. **B** Axial T1weighted image with fat suppression obtained during arterial phase image after contrast administration. The mass shows peripheral hypervascularity (*arrow*) as well as enhancement of the internal architecture. EUS findings were suggestive of SCA, and fluid aspiration was hypocellular; therefore, surgery was not performed initially. However, on follow-up MR examination, the mass increased in size and biopsy revealed

resection—i.e., pancreatoduodenectomy/distal or leftsided pancreatectomy vs. central pancreatectomy) and laparoscopic vs. open resection. Cysts with low malignant potential such as cystic neuroendocrine neoplasms or smaller side-branch IPMN may be treated by enucleation. If enucleation is considered, the cyst location relative to the MPD is of critical significance. Unintentional violation of the MPD leads to major post-operative pancreatic fistula that is unlikely to heal without a second major intervention (operation). Currently, many pancreatectomies are performed laparoscopically. Certain features such as local invasion of surrounding structures (kidney, adrenal, and stomach) may prompt neuroendocrine tumor. **C** A 64-year-old female presented with acute pancreatitis and was found to have a pancreatic cyst. Axial T2-weighted image without fat suppression shows multifocal cysts (*arrows*) within the tail. The largest cyst appears to have a T2 hypointense thick wall. **D** Axial post-contrast T1-weighted image with fat suppression. There is rim enhancement of the largest cystic component (*arrow*) without internal enhancement. The patient underwent distal pancreatectomy, and a low-grade cystic neuroendocrine tumor was found.

the surgeon to proceed directly to open operation. Crosssectional imaging helps identify cyst relationship to the splenic hilum and splenic vessels, important information for preoperative planning.

A close working relationship between radiologist and surgeon facilitates optimum patient care. The surgeon provides important clinical information regarding specific clinical questions, while the radiologist's "expert eyes" are crucial to interpret MRI studies. MRI is an essential imaging tool for the evaluation pancreatic cysts, providing important information that is useful diagnostically, for treatment planning, and for ongoing patient surveillance.



Conclusion

Cystic lesions of the pancreas constitute a diverse category included inflammatory lesions as well as neoplasms, including benign lesions, low-grade indolent neoplasia, and frankly malignant tumors. MRI with MRCP is a very useful diagnostic tool, but even with high-quality imaging, definitive characterization can be difficult, as Fig. 7. Lymphoepithelial cyst. A A 65-year-old male presented with abdominal pain and diarrhea. The patient was found to have a pancreatic cyst by CT. Coronal T2-weighted image without fat suppression demonstrates an exophytic and septated cyst with a thick wall (*arrows*) arising from the pancreas (*P*). There is relatively decreased T2-weighted signal therefore does not appear to be a simple cyst. B Axial T1weighted fat suppressed image before the contrast administration shows that fluid within the cyst has varying degree of increased signal (*arrows*). C Axial T1-weighted contrast-enhanced image with fat suppression. The cyst was deemed non-enhancing since there was no significant signal difference compared to pre-contrast image. A diagnosis of lymphoepithelial cyst was established following surgery.

there is substantial overlap in the appearance of most of the entities. There are a few characteristic imaging features such as the microcystic architecture and central scar seen typical of SCA, communication with the MPD seen in some side-branch IPMNs or debris seen with pseudocysts. MCNs are almost exclusively diagnosed in females. The diagnosis of MCN, which depends on the presence of ovarian-like stroma, requires histopathologic evaluation of the resected specimen. In the absence of a surgical specimen, evaluation for communication of a lesion with the pancreatic duct is the single best distinguishing feature for differentiation of MCN from sidebranch IPMN. Ductal dilation may provide evidence of chronic pancreatitis, but it may also indicate that an IPMN is of the main duct or mixed type. These types of IPMN are more likely to be malignant than the more common side-branch type; therefore, EUS-guided FNA may be necessary in these patients.

The decision to follow rather than resect a pancreatic cystic lesion is a matter of clinical judgment based on the age of the patient, comorbidities, and estimation of the cancer risk in the lesion. Important factors to consider include whether or not there is local or global dilation of the pancreatic duct, a clinical history suggesting pancreatitis, whether the cyst is solitary or multilocular, and the gender of the patient. Abdominal pain in a patient can itself be difficult to characterize; if it is suggestive of pancreatic pain, then it may indicate that a patient may have pancreatitis and that a cystic lesion may be inflammatory; it may also indicate that a mucinous lesion may be of a worrisome histology.

Minimally invasive procedures such as EUS and fluid aspiration for cytologic evaluation may be appropriate, even though these studies may also not be conclusive. Further investigation and long-term prospective studies are required to further clarify diagnostic criteria and provide standards for patient management, and to achieve a consensus regarding the duration and time interval for follow-up of patients with cystic lesions of the pancreas.

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