Cystic pancreatic lesions: From increased diagnosis rate to new dilemmas

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Abstract Cystic pancreatic lesions vary from benign to malignant entities and are increasingly detected on cross-sectional imaging. Knowledge of the imaging appearances of cystic pancreatic lesions may help radiologists in their diagnostic reporting and management. In this review, we discuss the morphologic classification of these lesions based on a diagnostic algorithm as well as the management of these lesions.

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Recently, multiple technological advances in imaging have significantly increased the detection and characterization of pancreatic cystic lesions [1–4]. With this increased sensitivity, comes the challenge of managing incidentally discovered pancreatic cystic lesions. While solid pancreatic tumors are almost invariably treated surgically, cystic lesions are currently most problematic. Indeed, the differential diagnosis of these cystic lesions ranges from benign (pseudocysts, serous cystadenomas) to potentially or frankly malignant lesions (intraductal papillary mucinous neoplasms, mucinous cystic neoplasms, cystic neuroendocrine tumors) [5–7]. To help patient’s treatment and follow-up stratification, several professional societies have proposed guidelines for the management of cystic pancreatic lesion [8–17]. In this review, we discuss the morphologic classification of cystic pancreatic lesions based on a diagnostic algorithm as well as the management of these lesions.

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**MRI protocol for pancreatic cystic lesions**

**Patient preparation**

To ensure gall bladder distention and limit bowel peristalsis, patient should fast at least 4 hours before the MRI examination.

Negative oral contrast is helpful in reducing the signal from the overlying stomach and duodenum. Pineapple or blueberry juices are commonly used. The manganese content of these juices results in an increased signal on T1-weighted imaging (WI) and a reduced signal on T2-WI.

**Protocol**

An optimal MRI evaluation of the pancreas requires a combination of single-shot T2W sequences, dynamic three-dimensional (3D) unenhanced and contrast material—enhanced T1W gradient-echo (GRE) sequences and MR cholangiopancreatography sequence (MRCP) [18–21].

In pancreatic cystic lesion assessment, the MRCP sequence is particularly important to evaluate the lesion communication with the pancreatic duct. The underlying principle behind MRCP is the use of T2W sequences with a very long TE so that only fluid signal ( bile and pancreatic juices) have sufficient signal to contribute to the image [21–24].

**Diagnostic algorithm**

Several questions are required to include the correct differential diagnosis of a cystic pancreatic lesion (Fig. 1).

**Is the lesion cystic?**

On CT, low attenuating lesion, such as lipoma [25–27], thrombosed splenic vein aneurysm or early adenocarcinoma [28] may mimic a cystic lesion. The lack of T2 hyperintense signal on MRI may steer us to the correct diagnosis. In contrast, a small non-enhancing T2 hyperintense lesion within the pancreatic head at the border of the duodenum may represent a fluid filled diverticulum [29]. The "blooming" T1 artefact caused by air may be lacking if the diverticulum is fluid filled and CT may help at the correction diagnosis.

**Is the lesion communicating with the main pancreatic duct?**

The transition from 2D MRCP sequences to 3D acquisition has resulted in more effective detection of communications between the cyst and the main pancreatic duct [30]. Intraductal papillary mucinous neoplasm and pseudocyst are the two pancreatic cystic lesions that potentially demonstrate a communication with the pancreatic duct system.

**Intraductal papillary mucinous neoplasm**

Intraductal papillary mucinous neoplasm (IPMN) is a mucin-producing lesion usually affecting men in their 6th to 8th decades and arising from the epithelium of the pancreatic duct (main duct type), its side branches (side branch type), or both (combined type) [8,31–44]. IPMNs are tumors composed of papillary proliferations of mucin-producing epithelium that cause excessive mucus production and cystic dilatation of the pancreatic ducts. Thus, the ductal dilatation observed is not due to a stenosis found in chronic pancreatitis or pancreatic adenocarcinoma, but rather due

![Figure 1. Decision algorithm for pancreatic cystic lesion diagnosis (IPMN: intraductal papillary mucinous neoplasm; MCN: mucinous cystadenoma; NET: neuroendocrine tumor; SPEN: Solid and papillary epithelial neoplasm; FNH: focal nodular hyperplasia).](image-url)
to an excessive production of mucin [45]. IPMNs range from non-invasive neoplasms with varying degrees of epithelial dysplasia to foci of carcinoma in situ and frankly invasive adenocarcinoma.

**Diagnosis**

MRI is the modality of choice for characterizing IPMNs as it provides better depiction of ductal communication than CT. Side branch IPMN: the diagnosis is mostly dependent on identifying the typical morphologic appearance (round or lobulated cyst) and communication between the lesion and the pancreatic duct.

On CT, a side branch IPMN appears most commonly as a hypodense, lobulated lesion in close proximity to the pancreatic duct which can occur anywhere in the pancreas. The main pancreatic duct is usually not dilated [46,47].

On MRI, side branch lesion appears as a small round or oval lobulated T2 hyperintense lesion. The morphology varies from a macrocystic pattern in which there is a unicellular or multilocular cyst with few septa to a more microcystic pattern in which multiple thin septa separate small cystic spaces (Figs. 2 and 3). Approximately 30% of side branch IPMNs are multifocal [5–7], unlike other cystic pancreatic neoplasms that are most often solitary. Thus, when multiple cysts lesions are present, IPMN is the most likely diagnosis.

Main duct IPMN usually shows focal or diffuse dilatation of the main duct (Fig. 4). Mucin products within the duct, dilated major or minor papilla bulging into the duodenal lumen and parenchymal atrophy may be present [16,38,48].

Combined type lesions show dilatation of both the main duct and side branch IPMNs.

**Suspicious findings**

As discussed earlier, the histologic appearances of IPMNs range from adenomas to carcinomas. Main duct IPMNs are highly likely to have associated malignancy (60–70%), whereas the risk is lower in isolated side branch lesions (15–20%). Multiple studies have tried to clarify specific CT and MR imaging features that would help differentiate invasive lesions from non-invasive ones [23,32–34,38,42,49,50].

Risk factors for malignancy depicted on imaging include:

- main duct caliber greater than 6–10 mm;
- increasing size of side branch lesions;
- side branch lesions larger than 3 cm;
- mural nodules and solid enhancing components.

**Management**

Treatment of IPMN involving the main pancreatic duct is surgical resection.

The treatment of side branch lesions without malignant features is controversial, especially lesions in asymptomatic elderly patients. Indeed, among side branch IPMN, almost 75–90% of them are stable in size and morphology at long-term follow-up and of those that do progress, the mean time interval for significant growth is longer than 2 years [51]. Thus, several professional societies have proposed guidelines for the management of these lesions based on high-risk CT/MRI features and lesions size [8,10–14,52,9]. For instance, the controverted American College of Radiology recommends no further follow-up for cysts smaller than 2 cm that remain stable over a year [15]. In contrast, the guidelines from the International Association of Pancreatologists recommend continuous follow-up even for lesions less than 2 cm [9]. Ironically, it is not the high-risk lesions which are the most difficult to manage, but the lesions without worrisome features that measure less than 3 cm. Indeed, the optimal time interval between follow-up examinations for these lesions remains to be determined. Recently, an increasing number of studies have shown that small branch duct IPMNs have malignant potential with an incidence of malignancy up to 20% even when < 3 cm in diameter [53,54]. However, the rate of malignancy in retrospective studies probably overestimates the true rate of malignancy in all patients with newly diagnosed IPMN. Nevertheless, this observation is in accordance with the European expert consensus statement of 2013, which reported that there was no safe lower size limit that completely excludes malignancy [16]. In Fig. 5, we propose a management algorithm derived from Fukoda guidelines and the American gastroenterological association taking in account both worrisome features and lesions size [17,9].

**Pseudocyst**

Pseudocysts account for around 20% of the cystic lesions of the pancreas. They occur in the setting of acute and chronic pancreatitis. Alcohol consumption may be in the patient background. The cyst is a result of hemorrhagic fat necrosis and encapsulation of pancreatic secretions in a fibrous capsule. Their imaging appearance evolves over time as they are initially ill-defined but later become well-circumscribed.

![Figure 2.](image_url) Coronal T2 (a) and MRCP sequence (b) showing a small T2 hyperintense lobulated lesion (arrowhead) communicating (arrow) with the main pancreatic duct consistent with a side branch IPMN (intraductal papillary mucinous neoplasm).
and if vascularized elements are seen within a cystic lesion on contrast-enhanced MR images, the lesion is not a pseudocyst.

The primary mimic of a pseudocyst is a mucinous cystic neoplasm or IPMN; in difficult cases, endoscopic ultrasound may help in the differential diagnosis. Pseudocyst demonstrates elevated amylase level in contradistinction to MCN and IPMN [55].

What is the cyst morphology?

Is the cyst microcystic?

**Serous microcystic cystadenoma**

Serous microcystic adenoma (SCA) have been reported to account for around 20% of pancreatic cystic tumor and mainly affects old women (8F:1M, 60 years old). They may be multiple in patients with Von Hippel-Lindau disease [56—58].

Usually discovered incidentally, the tumor is benign and does not require surgical treatment. There is a slight predominance of occurrence in the pancreatic head, but the lesion can occur throughout the pancreas.

Typically, they have a ''sponge like'’ or ''honey comb’’ appearance characterized by innumerable small cysts (less than 2 cm—more than 6 cysts) with a central stellate fibrous scar. The lesion does not communicate with the main pancreatic duct [57].

On CT, serous microcystic adenomas appear as a lobulated hypodense mass, often with central coarse calcifications and fibrosis (Fig. 7). After contrast injection, the central fibrous portions of the lesion enhance [57]. The lesion may demonstrate a more solid appearance [58] after contrast administration when there is a large number of very small cysts. In this later case, MRI may help in their diagnosis showing the T2 hyperintense signal of these cysts.

On MRI, the lesion demonstrates a cluster of tiny T2 hyperintense cysts associated with an hypointense T2-WI central scar (Fig. 7). After gadolinium injection, enhancement of the fibrous septations may be seen on early and late phases of imaging, with persistent enhancement of the central scar on more delayed phases of imaging. Again, there is no communication with the pancreatic ductal system and the main pancreatic duct is normal unless compressed by a large SCA [5,6].

Is the cyst macrocystic?

**Serous macrocystic cystadenoma**

Thirty percent of serous cystadenoma may take a more macrocystic appearance with fewer and larger cysts measuring between 2 to 7 cm or even may present as a single large cyst [48]. The central scar and/or fibrous components may be lacking. Like their microcystic variant, serous macrocystic adenoma are benign, and do not require surgical resection unless symptomatic [2,59].

Morphologically, it can be challenging to differentiate serous macrocystic cystadenomas from side branch IPMNs or mucinous neoplasms [60—63]. A retrospective study achieved a specificity of 100% in differentiating the lesion from a mucinous cystic tumor by using a combination of findings on contrast-enhanced CT: location in the pancreatic head, wall thickness < 2 mm, lobulated contour, and absence of wall enhancement [64].

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Figure 3. Axial T2-WI (a) demonstrates two large lobulated T2 hyperintense body and tail lesion (arrows). MRCP (b) shows the largest body lesion communicating with the main pancreatic duct (arrow). The mass (arrows) does not show internal complexity or enhancement after intravenous administration of a gadolinium chelate (arrows, c). The main pancreatic duct is not dilated. These features are consistent with side branch IPMNs (intraductal papillary mucinous neoplasms).
Endoscopic ultrasound (EUS) with fluid analysis can help to the diagnosis. In serous cystadenoma, cyst fluid amylase and CEA concentrations are very low, and a CEA concentration of less than 5 ng/mL virtually excludes a mucinous lesion [65,66].

**Mucinous cystic neoplasms (MCN)**

MCNs account for approximately 10% of pancreatic cystic neoplasms and occur mainly in women in their fifties (9F:1M; 50 years old). The most common locations are the pancreatic body and tail [67]. The lesion does not communicate with the pancreatic ductal system. Since mucinous cystadenomas have malignant potential, all lesions are considered surgical.

On CT studies, MCN presents as a multilocular well-circumscribed macrocystic lesion, with loculations larger than 2 cm. Enhancement of the cyst wall, septations or mural nodules can be seen [67].

On MRI, MCNs appear usually as a unilocular or mildly septated cystic T2-WI hyperintense lesion (less than 6 loculations measuring more than 2 cm each) with a T2 hypointense capsule. The T1-WI signal intensity may be variable based on the proteinaceous content of the cyst. After gadolinium injection, enhancement of the thick cyst wall is seen on more delayed phases of imaging because it is fibrous, with associated enhancing internal septations and areas of mural nodularity [5,6]. No communication with the pancreatic duct system is seen on the MRCP sequence (Fig. 8).

Differentiation between mucinous cystic adenocarcinomas and adenomas is not always feasible on imaging, but some findings such as wall thickening, papillary projections, mural nodules or peripheral calcifications may suggest malignant behavior [67,68].

EUS is particularly helpful in the prediction of malignancy. MCNs have a low amylase level (< 250 I/L) and a high CEA (> 800 ng/mL) and, when malignant, a high CA 19.9 level is measured.

**Cystic pancreatic endocrine neoplasm (CPEN)**

CPENs represent approximately 20% of all neuroendocrine tumors and 2% of pancreatic cystic lesions. They have equal gender predilection, with mean patient age of 50 years. They may be part of multiple endocrine neoplasia syndromes. CPEN most commonly occurs in the body and tail of the pancreas. Cystic pancreatic neuroendocrine tumors are less likely to be functional or symptomatic and are typically smaller than solid pancreatic neuroendocrine tumors [69,70]. Given their varying malignant potential, complete resection is the treatment of choice.

In keeping with the hypervascular nature of neuroendocrine tumors, imaging of CPEN typically shows on CT or
Figure 5. Proposed management algorithm of side branch IPMN (IPMN: intraductal papillary mucinous neoplasm; MPD: main pancreatic duct; EUS: endoscopic ultrasound).

MRI a septated cyst with a rim of thick arterially enhancing wall (Fig. 9) [71,72].

**Lymphoepithelial cyst**

Lymphoepithelial cysts are very rare cystic lesions of the pancreas. They usually measure less than 5 cm and are seen in men. The cysts are lined by squamous epithelium and surrounded by dense lymphoid tissue. Their imaging appearances vary and they may be either unilocular or multilocular. On EUS, they demonstrate a high level of CEA and lymphoid cells [73].

Is there any suspicious findings?

Is there a main duct dilatation or an increased duct dilatation?

The association of a pancreatic lesion with an upstream-dilated pancreatic duct is always suspicious of malignancy and usually requires histology sampling. In case of IPMNs on follow-up imaging, a change in the main pancreatic duct should be suspicious for underlying malignancy [34,38,42,49].

Are there mural nodules or a solid portion within the cyst?

Classically, solid component or mural nodules associated with MCNs and IPMNs suggest malignant potential and require surgery [34,38,42,49].
Cystic pancreatic lesions: From increased diagnosis rate to new dilemmas

**Figure 7.** Coronal (a) and axial T2-WI (b) demonstrate a well-defined large pancreatic lesion, consisting of a cluster of many small cysts (arrow, a) separated by thin septa. The central focal region of T2 signal hypointensity (arrowhead, b) from which the thin septa radiate is in keeping with a calcified scar as shown on CT (arrow, d). Axial delayed contrast-enhanced MRI (c) demonstrates thin enhancement of the internal septa (arrows). These are all features of benign serous cystadenoma.

**Figure 8.** Axial T2-WI shows well-circumscribed hyperintense lesion (arrow) in the tail of pancreas that does not show communication with pancreatic duct. The mass (arrows) does not show internal complexity or enhancement after intravenous administration of a gadolinium chelate (b). On contrast-enhanced image, there is subtle delayed enhancement of surrounding wall (arrow). These features suggest mucinous cystadenoma.
Two other cystic lesions may combine solid and cystic appearance.

**Solid and papillary epithelial neoplasm (SPEN)**

SPEN are very rare pancreatic tumors that occur almost exclusively in young women (9F:1M; mean age 25 years). SPENs are usually benign or of low-grade malignant potential. It is usually solitary and large at presentation, which occur within the body/tail of the pancreas [74,75].

On CT, SPENs generally appear as a well demarcated, encapsulated, large, mixed cystic and solid tumor. The solid tissue components are generally noted at the periphery, with central areas of hemorrhage. After contrast administration, the capsule and solid components enhance (Fig. 10) [74,75].

On MRI, SPENs shows a well-encapsulated mass that commonly has a heterogeneous appearance on both T1-weighted and T2-weighted imaging [76]. Areas of hemorrhage appear hyperintense on T1-weighted imaging, and hypointense on T2-weighted imaging. After gadolinium injection, progressive enhancement of the solid portions during the portal venous and delayed phases is usually noted. A key diagnostic finding of SPEN is the presence of a fibrous capsule that surrounds the tumor [77,78].

**Ductal adenocarcinoma with cystic degeneration**

Complex cystic areas representing internal tumor necrosis or side branch ductal obstruction may be seen associated with this classically solid ill-defined infiltrative tumor. Cystic changes are more commonly observed in large poorly differentiated adenocarcinomas [79]. The tumor usually causes vascular invasion and pancreatic ductal obstruction at an early stage and thus is well depicted on cross-sectional imaging; however, a more cystic appearance may be seen.

**How is the liver? Look outside the cyst**

Concomitant liver evaluation is critical as some specific features may be associated with cystic pancreatic lesions:

- pseudocysts may be related to acute alcoholic pancreatitis. Thus, dedicated liver evaluation for cirrhosis, dysplastic nodules or hepatocellular carcinoma is recommended;
- cystic neuroendocrine lesion, mucinous cystadenocarcinoma may be associated with cystic liver metastases (Fig. 11). Again, careful evaluation of the liver parenchyma is recommended;
- SPEN, MCN are usually seen in young or middle aged women who can present with liver adenoma and focal nodular hyperplasia.

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**Figure 9.** Cystic pancreatic endocrine neoplasm: axial T2-weighted image (a) T2-WI showing a well-circumscribed unilocular hyperintense lesion (arrow) in tail of pancreas. On enhanced sequence, the mass shows avid rim enhancement (arrow) in early arterial phase image (b), persistent on portovenous phase (arrow, c).

**Figure 10.** Axial contrast-enhanced CT image shows 6-cm hypovascular, well-circumscribed mass in body and tail of pancreas with internal nodularity (arrowhead) and thick enhancing wall (arrow) in keeping with a solid and papillary epithelial neoplasm.
Cystic lesions: From increased diagnosis rate to new dilemmas

### Table 1

<table>
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<tr>
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<th>IPMN</th>
<th>SPN</th>
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**Figure 11.** Summary of the different cystic lesion of the pancreas (SCN: serous cystadenoma; MCN: mucinous cystadenoma; IPMN: intraductal papillary mucinous neoplasm; SPN: solid and papillary epithelial neoplasm; PEN: pancreatic endocrine neoplasm; CP: chronic pancreatitis; EUS: endoscopic ultrasound).

### Conclusion

Cystic tumors of the pancreas are increasingly discovered on cross-sectional imaging. Accurate assessment of these lesions is important for treatment management. Besides IPMN guidelines varying widely from institution to institution, the increased understanding of this pathology and clinical course has helped better patient management. Recent genetic analyses have demonstrated that GNAS mutation and G-protein signalling may play a crucial role in IPMN progression. Future imaging studies on radiogenomics may create new imaging biomarkers that could better identify IPMN progression.

- Serous microcystic adenoma include usually more than 6 cysts in number, measuring less than 2 cm in contradistinction with mucinous adenoma which demonstrates fewer number of cyst but larger cyst.

### Take-home messages

- Most of these cysts are incidental findings and are benign or low-grade neoplasms.
- Multiple cystic lesions within the pancreas, which communicates with the main pancreatic duct, are characteristics of side branch IPMNs.
- Risk factors for malignancy in IPMN include: main duct caliber greater than 6–10 mm, increasing size of side branch lesions, side branch lesions larger than 3 cm, mural nodules and solid enhancing components.

### Disclosure of interest

The authors declare that they have no competing interest.

### References


