Pancreatic cystic neoplasms - A pictorial review

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Authors: J. Adu, A. McLean, A. Parsai, K. L. Shahabuddin; London/UK
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Learning objectives

- To illustrate the characteristic imaging features of different types of cystic pancreatic lesions
- Discuss the role of endoscopic ultrasound in the diagnosis and management of pancreatic lesions
- To discuss the appropriate imaging surveillance of selected cystic pancreatic lesions.
Background

The World Health Organisation (WHO) classifies cystic neoplasms of the pancreas into three main categories: benign, borderline (potentially malignant) and malignant\textsuperscript{1,2}. The major histologic subtypes include serous cystic neoplasms, mucinous cystic neoplasms (MCN), intraductal papillary mucinous neoplasms (IPMN), solid pseudopapillary neoplasms (SPPN) and cystic pancreatic neuroendocrine tumours\textsuperscript{3}. Rarer types include cystic ductal adenocarcinomas and acinar cell cystadenomas.

Currently, all cystic neoplasms are considered to be at the very least borderline malignant with the exception of SCN which are almost always benign\textsuperscript{3} although isolated cases of malignant SCN have been reported\textsuperscript{4}. The pancreatic pseudocyst is the most important non-neoplastic cystic lesion to consider as it is fairly common and its definitive management is entirely different from cystic neoplasms of the pancreas, therefore it will be covered in this review.
Findings and procedure details

Imaging plays a crucial role in the detection and characterization of cystic lesions of the pancreas. Technological innovations in MDCT and MRI have led to improvements in analysis and morphologic differentiation of cystic pancreatic lesions and are widely considered to be the primary imaging modalities in the care of patients with cystic lesions of the pancreas.

**Pseudocyst**

Pseudocysts are pancreatic or peri-pancreatic fluid-filled collections that are encapsulated by fibrous tissue and usually form after inflammation, necrosis or haemorrhage related to acute pancreatitis or trauma. In acute pancreatitis, there is usually associated mesenteric oedema and peri-pancreatic stranding, whereas in chronic pancreatitis, there may be associated pancreatic parenchymal calcification. Older cysts tend to have thicker walls that may contain calcium. These cysts can be located anywhere within the pancreas but predominantly involved the body or tail.

Unenhanced CT usually shows a pancreatic pseudocyst as a round or oval hypodense lesion (Figure 1). If the pseudocyst contains haemorrhage, it appears as areas of increased attenuation within the lesion. On contrast enhanced CT, the wall of a pseudocyst enhances but not the fluid within it (Figures 2 and 3).

On unenhanced T1-weighted images, the lesion is hypointense unless it contains haemorrhage elements that are high signal. A pseudocyst appears hyperintense on T2-weighted sequences and has homogenous bright internal signal intensity, a characteristic feature that confirms that the lesion is a fluid-filled structure (Figure 4).

**Mucinous Cystic Neoplasms and Mucinous Cystadenomas**

Mucinous cystic neoplasms (MCNs) are the most common cystic neoplasm and occur most frequently in middle-aged women (>95%) and in the distal pancreas (>95%).\(^5\) Histologically, they are characterized by dense, ovarian-like stroma that surrounds the tumour, and an inner-epithelial layer with tall, mucin-secreting cells. Owing to their potential to grow very large in size and their malignant potential\(^6\) (mucinous cystadenocarcinoma, 17.5%) surgical resection is the mainstay of treatment\(^7\). Most are incidental findings with the remainder presenting with non-specific abdominal symptoms including weight loss in metastatic cases.
On CT, MCNs are unilocular or multilocular, well-defined smooth lesions that are hypodense to surrounding pancreatic parenchyma. The cystic contents have fluid density. Contrast-enhanced scans show enhancement of the cyst wall (Figure 5) and accentuate any septations and mural nodules. The presence of mural nodules or septal thickening and calcification strongly suggest a malignant lesion. Peripheral calcification is present in approximately 16% of cases (Figure 6). Distal to the tumor, the pancreas may show such changes of chronic pancreatitis such as atrophy, duct dilatation, coarse calcification and areas of decreased enhancement, although such changes are not specific for mucinous neoplasms. It is essential to look for evidence of invasion into surrounding organs.

Compared with the serous cystic tumours, cyst fluid CEA is elevated in mucinous cystic tumours and the degree of elevation correlates with the diagnosis of mucinous cystadenoma or mucinous cystadenoma with malignant potential (Figure 7). Serum tumour markers CA 125 and CA 72-4 are also suggestive of a malignant or pre-malignant lesion (Figure 8). Mucinous cystadenomas can grow to be very large in size if left untreated (Figure 8).

**Serous Cystadenomas (SCN)**

SCNs are composed of multiple small cysts, which are conjoined in a honeycomb-like pattern. The cysts are lined by glycogen-rich cuboidal epithelium, separated by fibrous septa that radiate out from a central scar which may be calcified. SCNs can exhibit macroscopic variations in locule size and are now subdivided into (a) serous microcytic and (b) serous oligocystic adenomas. Malignant change, although reported, is extremely rare, and therefore the condition is considered to be benign. There is a female predilection, and occurrence is mostly in the seventh decade of life. Lesions are most commonly seen in the pancreatic head. Transabdominal ultrasound of SCNs demonstrates a hypoechoic lobulated lesion (Figure 9).

On CT, a serous cystadenoma commonly has a lobular shape and appears hypodense on unenhanced scan because of its water-density nature. The fibrous portion of the lesion enhances after contrast administration (Figure 10). Calcified areas usually appear hyperdense and are generally arranged in a characteristic stellate pattern in the centre of the lesion (Figure 11). The characteristic honeycomb appearance is seen in only 20% of cases. In general, the appearance of an SCN depends on the number of fibrous septations and their degree of enhancement.

On MRI, an SCN appears as cluster of small cysts on T2-weighted images. The cystic components of an SCN are high signal, and the fibrous elements are low signal. On unenhanced T1-weighted imaging, the cystic portion of the tumour is hypointense.
The fibrous components are hypointense on all unenhanced sequences. After contrast administration, enhancement of the fibrous elements may be detected on early and late imaging, with persistent enhancement of the central scar on delayed dynamic imaging (Figure 12).

The visualization of four of the five following CT and MRI features have been report to facilitate diagnosis of SCN\textsuperscript{10}: (i) location in the pancreatic head, (ii) wall thickness <2mm, (iii) lobulated contour, (iv) lack of communication with the pancreatic duct and (v) minimal wall enhancement.

**Solid Pseudopapillary Neoplasm**

SPNs of the pancreas are uncommon and comprise <4% of resected pancreatic tumours. They also predominantly affect women (>80%) in their 30's\textsuperscript{11,12}. SPNs can be located throughout the pancreas; they are detected as incidental findings or because they cause symptoms such as abdominal pain, pancreatitis, jaundice or a palpable mass. Malignant potential is low\textsuperscript{11}.

On CT, SPNs appear a large encapsulated mass with cystic and solid component. Cystic components are secondary to tumour degeneration. The solid tissue elements are situated peripherally, with central areas of haemorrhage and cystic degeneration with internal branching papillae. The solid components enhance after contrast administration (Figure 13).

MRI imaging of SPNs show a well-defined mass that most commonly has a heterogenous appearance due to haemorrhage of both T1- and T2 weighted sequences. Areas of intralesional haemorrhage are hyperintense on unenhanced T1-weighted sequences, and hypointense on T2 weighted scans (Figure 14). An important diagnostic feature of SPNs is the presence of a low signal fibrous capsule, which most probably develops are a reaction to the expansile tumour. The enhancement pattern shows a gradual accumulation of contrast agent within the tumour, differentiating it from neuroendocrine tumours, which show early arterial enhancement.

**Neuroendocrine tumours**

Neuroendocrine tumours, or islet cell tumours, account for 1-5% of all neoplasms\textsuperscript{13}. Patients are typically in their 50’s, with a slight male predominance. Most are solitary lesions that arise sporadically, but may also occur as part of genetic syndromes, such a multiple endocrine neoplasia type 1 (MEN1), von Hippel Lindau, neurofibromatosis type 1 and tuberous sclerosis. Neoplasms in these conditions are often multiple, particularly
in MEN1. Islet tumours are also classified as function and non-functional, depending on whether the cell secrets hormones. Functional tumours include insulinomas (present with hypoglycaemia) and gastrinomas (present with peptic ulcer in Zollinger-Ellison Syndrome).

Transabdominal ultrasound imaging of neuroendocrine tumours will demonstrate the lesion to be isoechoic (Figure 15). On CT, neuroendocrine tumours are hyperattenuating and may be within the gland or exophytic (Figures 16 and 17). These rarely cause pancreatic duct or obstruction. The most useful discriminator of malignant risk is tumour size with 90% of tumours under 20mm being benign and 71% over 20mm being malignant.

Neuroendocrine lesions do not characteristically show calcification, and as lesions grow they develop cystic or necrotic areas. The periphery of the lesion will continue to enhance arterially. Local vascular encasement or invasion, which is commonly seen with ductal adenocarcinoma, is rarely seen with neuroendocrine tumours. Arterial phase imaging of the liver is vital to detect hepatic metastases.

**Intraductal Papillary Mucinous Neoplasm**

IPMN is a mucin-producing tumor of the pancreas that clinically and histopathologically distinct from mucinous cystadenoma. These are most frequently seen in men (mean age 60 years) and are characterised by mucinous transformation of the pancreatic ductal epithelium. IPMNs can be classified according to whether the disease process involves the main pancreatic duct (M-IPMN), isolated branch ducts (BD-IPMN) or a combination of both. The location of the tumour is important for the prognosis. M-IPMNs are likely to undergo malignant transformation (70%), while 15-20% of BD-IPMNs have malignant potential.

The imaging diagnosis of IPMN depends of identifying the relationships of the lesion to the pancreatic duct, especially in the case of branch duct types. On CT, a BD-IPMN typically appears as a hypodense non-enhancing pleomorphic lesion. It is classically located in the uncinate process and in close proximity to a non-dilated main pancreatic duct. (Figure 18). Main pancreatic duct lesions can be classified according to whether they produce diffuse or segmental duct dilatation (Figure 19). The cystic nature of IPMNs is often better appreciated on MRI (Figures 20 and 21).

**The Role of Endoscopic Ultrasound Scan (EUS)**
EUS is an excellent imaging technique for detecting signs predictive of malignancy or aggressiveness in cystic pancreatic lesions. Such signs include internal septations, mural nodules, solid masses, vascular invasion and lymphatic metastasis\textsuperscript{15,16} (Figure 22). Furthermore, EUS can be used for sampling fluid and solid components and depicting debris and wall thickness\textsuperscript{17}.

EUS has been shown to have sensitivity, specificity and accuracy as high as 90.5\%, 86.2\% and 88\% respectively for differentiating cystic from solid pancreatic lesions\textsuperscript{18}. However, EUS is invasive and operator dependent, and these limitations have may lead to variability in determining in accurately differentiating between benign and malignant lesions\textsuperscript{15,17}. Furthermore, it can be technically challenging to sample lesions smaller than 3cm\textsuperscript{15,17}. Currently, EUS with or without aspiration is used in the following instances: indeterminate lesions on cross sectional imaging; care of patients who are at high surgical risk owing to comorbidities or advanced age, which precludes them from undergoing extensive surgery; and confirming the malignant status of a lesion prior to resection.

EUS-guided cyst fluid aspiration is often performed in conjunction with EUS for definitive diagnosis. Biochemical analysis of the fluid aspirate for estimation of carcinoembryonic antigen (CEA), mucin and amylase concentrations can facilitate reliable differentiation of mucinous from non-mucinous neoplasms\textsuperscript{19}. A high level of cyst fluid amylase concentration is also helpful in differentiating pseudocysts from lesions that are not pseudocysts\textsuperscript{19}.

**Management and Surveillance of Cystic Pancreatic Lesions**

Surgery is often recommended for symptomatic cystic lesions, cystic lesion having complex morphological features (e.g. solid components) and cystic lesions detected in patients under 50 years\textsuperscript{20}. A panel of experts have proposed the Sendai guidelines for the management of IPMNs. These guidelines recommended surgical resection of all main duct IPMNs due to the high malignant potential\textsuperscript{20}. Resection of branch duct IPMNs (BD-IPMN) is recommended if the lesion is symptomatic, larger than 3cm, or mural nodules or main duct dilatation is present\textsuperscript{20}. Lesions less that 3cm that do not exhibit the suspicious features outlined above can be kept under surveillance. The follow-up guideline varies in accordance with the size of the BD-IPMN. Lesions smaller than 1cm are evaluated annually; those measuring 1-2cm are reviewed every 6-12 months, and those measuring 2-3cm are imaged at 3-6 month intervals\textsuperscript{20}.

The choice of imaging modality for monitoring IPMNs depends of institutional preference and the patient's age. Although CT an MRI are both accepted methods for follow-up
of these lesions, for adults younger than 50 years, MRI is preferred over CT owing to concerns about exposure to ionizing radiation. 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.
Fig. 1: Axial unenhanced CT of a pancreatic pseudocyst arising from the body/tail of the pancreas following pancreatitis in a 30 year old male.

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Fig. 2: Axial post-contrast CT image of a 30 year-male demonstrating enhancement of the thick wall of a pancreatic pseudocyst (arrows).

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**Fig. 3:** Coronal post-contrast CT image demonstrating a pancreatic pseudocyst (yellow arrow) with marked surrounding inflammatory changes (blue arrow).

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Fig. 4: MRI axial images of a 28 year-old female with a pancreatic pseudocyst secondary to pancreatitis. (A) T1-weighted image demonstrating low signal intensity of the lesion (yellow arrows). (B) The corresponding T2 weighted image illustrates homogenous hyperintense signal of the pseudocyst (blue arrows).

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Fig. 5: Axial CT images of 56 year-old male with an asymptomatic mucinous cystic neoplasm of the pancreatic tail. (A) Unenhanced imaging demonstrates a smooth walled, unilocular lesion (red arrows) with a tiny fleck of calcification (yellow arrow). (B) Post contrast imaging illustrates enhancement of the cystic wall (blue arrows).

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Fig. 6: Contrast-enhanced axial CT image of a 33 year-old female with a 3cm mucinous cystic neoplasm of the tail of the pancreas (blue arrows) with calcification of the lateral wall (yellow arrow).

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Fig. 7: Contrast enhanced axial CT image of 33 year-old female demonstrating a multi-loculated cystic lesion arising from the body/tail of the pancreas (red arrows). Biochemical analysis of the pseudocyst fluid aspirate showed a CEA level of over 2000, confirming the diagnosis of a mucinous cystic neoplasm.

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Fig. 8: Large cystadenocarcinoma (long arrow) in an 80 year-old male. Note the irregular soft tissue septation (short arrow). Mass causes biliary obstruction with a distended gallbladder (GB) and intrahepatic ducts (arrowhead).

Fig. 9: Transabdominal ultrasound scan demonstrating a serous adenoma of the head/uncinate process of the pancreas demonstrating its multiloculated, hypoechoic appearance.

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**Fig. 10:** Axial CT images of a 71 year-old female with a 5.2cm serous cystadenoma of the uncinate process of the pancreas. (A) Pre-contrast image demonstrates a multiloculated cystic lesion with a lobulated contour (yellow arrows). (B) Magnified, post contrast imaging show enhancement of the fibrous septations within it (blue arrows).

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**Fig. 11:** CT images of a serous cystadenoma. Axial (A) and coronal (B) contrast enhanced images show serous cystadenoma of the pancreatic head with classic appearance of lobulated outline, fine internal septations, lack of vascular encasement, and calcification of central scar (arrows)

**Fig. 12:** MRI of serous cystadenoma. (A) Heavily T2-weighted coronal thick slab MRP shows high-signal lesion (white arrows) at junction of head and body of pancreas (cluster of small cysts). Internal septations is best depicted on MRCP image. (B) Dynamic delayed coronal reconstruction image after gadolinium injection shows that the lesion (black arrow) has homogenous low signal with rim enhancement and contains fine septations.


**Fig. 13:** Triple phase CT images of a 39 year-old female with a 3.2cm solid papillary neoplasm of the body of the pancreas. (A) Pre contrast axial image demonstrates a low density lesion (yellow arrow) in comparison the pancreatic parenchyma. (B) The arterial phase study illustrates enhancement of the tumour wall (red arrows). (C) The delayed phase demonstrates enhancement of the solid components of the mass (blue arrow). (D) Delayed phase, coronal image of the same patient as Figures 9A, B and C.

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Fig. 14: T2-weighted axial MRI image demonstrating features typical of a SPN in the head/neck of the pancreas with mixed solid (single arrow) and cystic (double arrows) components.

**Fig. 15:** Transabdominal ultrasonography of 3x3cm ovoid, isoechoic soft tissue mass in the region of the pancreatic head, which was confirmed to be a neuroendocrine tumour on subsequent cross sectional imaging.

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Fig. 16: Axial CT image showing an arterially enhancing insulinoma (blue arrow) in a 75 year-old woman with hypoglycaemia.

**Fig. 17:** Axial (A) and coronal (B) arterial CT images showing an arterially enhancing insulinoma in the uncinate process of a 76-year old male.


**Fig. 18:** CT images of a 72 year-old male with an asymptomatic branch-duct IPMN of the pancreatic head. (A) Unenhanced imaging shows a low density pleomorphic lesion (yellow arrows) which does not enhance after administration of IV contrast (B).

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Fig. 19: Contrast enhanced axial CT image showing a grossly distended main pancreatic duct (yellow arrow) in an 83 year-old male with a main duct IPMN.

**Fig. 20:** MRI images of a 72 year-old male with an asymptomatic branch duct intraductal papillary mucinous neoplasm of the pancreatic head. (A) Axial T1-weighted image shows a hypointense lesion (yellow arrows). (B) Axial T2-weighted image shows a hyperintense cystic lesion (red arrows) that communicates with the main pancreatic duct (blue arrow).

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**Fig. 21:** Axial T2-weighted contrast enhanced MR image of a branch duct intraductal papillary mucinous neoplasm of the pancreatic head showing high signal cystic lesion (yellow arrow) that communicates with the main pancreatic duct (blue arrow).

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Fig. 22: Endoscopic ultrasound image of a solid pseudopapillary neoplasm demonstrating solid and cystic components.

Conclusion

Cystic lesions of the pancreas are increasingly detected, especially in asymptomatic patients due to imaging studies performed for other indications. A wide spectrum of disease entities have been recognized which may present as a cystic lesion of the pancreas which can range from obviously benign to indeterminate to borderline malignant potential lesion to overt malignancy. The role of imaging in detecting the lesions and confirming its location and proximity to surrounding structures is well recognized, and CT or MRI is ideally suited for this purpose. Different pathological subtypes have distinct features on imaging; therefore radiologists need to be familiar with their different appearances in order to facilitate diagnosis. EUS including EUS-guided aspiration for cytology and fluid studies has proven to be a useful addition to aid in the diagnosis of cystic lesions of the pancreas.


