

Mistakes in pancreatic cystic neoplasms and how to avoid them

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Pancreatic cystic neoplasms (PCN) are a frequent and clinically challenging condition. PCN prevalence increases with age and reports estimate that they may be present in 2–45% of the general population^{1,2}. In addition, the biological behaviour of the various types of PCN differs (ranging from benign to malignant [Table 1]), requiring different surveillance and therapeutic approaches. Correct management of PCN is, therefore, critical for avoiding progression to cancer, but at the same time avoiding unneeded close and long-term follow-up, unnecessary invasive diagnostic procedures and overtreatment.

In this article, we discuss some frequent and relevant mistakes that can be made in the diagnosis, surveillance and management of PCN, and propose strategies to avoid them. These strategies are mainly based on the recently published European evidence-based guidelines on PCN.³



Image courtesy of J.E. Domínguez-Muñoz

type of PCN, and the CEA level should be considered only as an adjunct to imaging and the cytological features of the cystic lesion.

Mistake 3 Performing EUS-FNA for cytology in every cystic lesion

EUS-FNA (fine-needle aspiration) is only indicated when there are unclear CT and MRI findings and the EUS-FNA result is expected to change clinical management.³ Cyst fluid analysis should include amylase or lipase, CEA and cytology. Compared with EUS alone, cyst fluid cytology after EUS-FNA increases the accuracy for differentiating mucinous from nonmucinous and benign from malignant PCN; however, cytology is highly specific but insensitive in this setting.^{11,12,18}

Mistake 4 Long-term surveillance of every patient with PCN

Surveillance of PCN is determined by the risk of progression to cancer. Patients who have a definite diagnosis of serous PCN do not require surveillance owing to the benign nature of these lesions.^{19,20} By contrast, the risk of progression of mucinous PCN—both MCN and IPMN—to high-grade dysplasia and cancer increases over time. Therefore, if there is no indication for surgery, patients who have MCN or IPMN should be subject to long-term follow-up. Nevertheless, long-term surveillance is not indicated in patients who have MCN or IPMN if they are not fit for surgery because they have comorbidities.^{21–24}

Mistake 1 Evaluating every cystic pancreatic lesion to define the specific lesion type

Computed tomography (CT) scanning, magnetic resonance imaging and cholangiopancreatography (MRI/MRCP) are accurate methods for the detection of PCN, with MRI and MRCP being used most often. However, the accuracy of these methods remains relatively low for identifying the specific type of PCN.^{4–9} If a specific diagnosis is not established by cross-sectional imaging, further investigations are not indicated if the results will not change clinical management (e.g. if there is a clear indication or contraindication for surgery, or in cases where there are small cysts with no indication for surgery).³

Mistake 2 Relying on cyst fluid analysis to diagnose the specific type of PCN

Although cyst fluid carcinoembryonic antigen (CEA) and cyst fluid amylase or lipase increase the accuracy of endoscopic ultrasonography (EUS) for differentiating mucinous from nonmucinous PCN, the diagnostic accuracy of these biomarkers is too low to establish the specific PCN type.^{10–16} In addition, cyst fluid CEA does not allow the differentiation of mucinous cystic neoplasms (MCN) from intraductal papillary mucinous neoplasms (IPMN), nor benign mucinous cysts from those with high-grade dysplasia or cancer.¹⁷ Therefore, cyst fluid CEA is not reliable for the diagnosis of the specific

Pancreatic cystic neoplasm	Malignant potential
Mucinous	
Intraductal papillary mucinous neoplasms (IPMN)	Low to high
Mucinous cystic neoplasms (MCN)	Moderate to high
Nonmucinous	
Serous cystic neoplasms (SCN)	None
Solid pseudopapillary neoplasms (SPN)	Moderate
Cystic pancreatic endocrine neoplasms (CPEN)	Moderate

Table 1 | Types of pancreatic cystic neoplasm and their malignant potential.

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Mistake 5 Using CT scanning for surveillance of patients with PCN.

A multiphase pancreas protocol CT scan is highly accurate for the characterization of PCN. To qualify as a multiphase pancreatic protocol CT, an examination requires inclusion of thin reconstruction images (≤ 2.5 -mm slice thickness) obtained during the pancreatic parenchymal phase. Despite that, MRI/MRCP is preferred for surveillance to avoid repeated exposure to radiation during long-term follow-up. In addition, MRI/MRCP is more sensitive than CT scanning for the identification of relevant PCN features, such as mural nodules (which are associated with a high risk of high-grade dysplasia or cancer), internal cyst septations (that may be of help for the specific diagnosis of PCN), and the presence of multiple cysts (supporting the diagnosis of multiple side-branch IPMN).^{7,25-27}

Mistake 6 Surveillance of patients who have IPMN when there are appropriate indications for surgery

In patients who have IPMN and are fit for surgery there are several absolute indications for surgery—the presence of jaundice (tumour related), a positive cytology for high-grade dysplasia or cancer, the presence of a solid mass or a contrast-enhancing mural nodule of ≥ 5 mm, or the presence of a main pancreatic duct dilatation of ≥ 10 mm (figure 1).³ Surveillance of patients with IPMN who are fit for surgery is appropriate only in the absence of any surgical indication.²¹

In the presence of one relative indication for surgery (i.e. growth rate ≥ 5 mm/year, increased serum CA19.9 level in the absence of jaundice, main pancreatic duct diameter

Absolute indications

- Tumour-related jaundice
- Positive cytology for high-grade dysplasia or cancer
- A solid mass or a contrast-enhancing mural nodule of ≥ 5 mm
- A main pancreatic duct dilatation of ≥ 10 mm

Relative indications

- Growth rate ≥ 5 mm/year
- Increased serum CA19.9 level in the absence of jaundice
- Main pancreatic duct diameter of 5 to 9.9 mm
- Cyst size ≥ 40 mm
- New-onset diabetes mellitus
- Acute pancreatitis caused by IPMN
- Contrast-enhancing mural nodules of < 5 mm

Figure 1 | Indications for surgery in patients who have IPMN and are fit for surgery.

of 5 to 9.9 mm, cyst size ≥ 40 mm, new-onset diabetes mellitus, acute pancreatitis caused by IPMN, or contrast-enhancing mural nodules of < 5 mm), surveillance is acceptable for patients who have significant comorbidities or a short life expectancy, but not for those who have no significant comorbidities or two or more relative indications for surgery.³ It is also important to highlight that the greater the number of relative indications for surgery, the higher the probability of malignancy.^{28,29}

Mistake 7 Interrupting surveillance in patients who have IPMN or MCN that show no significant change after 3–5 years

As the risk of IPMN or MCN progressing to high-grade dysplasia or cancer increases over time, the chance of developing indications for surgery (whether they are clinical or based on imaging) also increases over time. Surveillance of patients who have IPMN or MCN but no indication for surgery should, therefore, not be interrupted as long as they are fit for surgery, even if no significant change is observed after 3–5 years.^{3,21-23,30}

Mistake 8 Operating too early or too late on patients who have IPMN

As the risk of cancer associated with IPMN is high for patients who have absolute or relative indications for surgery, resection of IPMN in those patients should not be delayed. By contrast, although malignancy cannot be definitively excluded before histological examination of a surgical specimen, the risk of high-grade dysplasia or cancer in patients with IPMN is low in the absence of risk factors.²¹ On that basis, and as a general rule, patients who have no indication for surgical resection (i.e. small cysts with no risk factors for malignancy) should not be operated on unless they develop an indication for surgery during follow-up. In this context, factors such as life expectancy, the patient's compliance and wishes, and the surgical risk are important for appropriate clinical decision making.

Mistake 9 Performing a parenchyma-sparing pancreatectomy in patients who have a surgical indication for IPMN

A parenchyma-sparing pancreatectomy is a nononcological procedure and has a morbidity comparable to, or even higher than, that of an oncological pancreatic resection.^{31,32} The procedure should not be carried out in patients who have a surgical indication for IPMN because

of their risk of cancer or high-grade dysplasia. The surgical approach for IPMN should be an oncological resection with standard lymphadenectomy.^{3,31,32}

Mistake 10 Ignoring long-term surveillance of patients who have undefined cysts

After an appropriate diagnostic work-up, small cysts may remain undefined in terms of their specific type. Despite that, an undefined cyst could be mucinous and the risk of malignant transformation may increase over time. For this reason, criteria for surgical resection or surveillance of undefined cysts may follow the same general rules defined for branch duct IPMN (BD-IPMN). Undefined small pancreatic cysts are, however, frequent and often have no effect on a patient's survival in the absence of any risk factor for malignancy.³³ On that basis, the European Study Group on Cystic Tumours of the Pancreas recommends that, in the absence of risk factors for malignancy, undefined cysts < 15 mm in size should be re-examined every year—if they are stable for 3 years, the follow-up may be extended to every 2 years as long as the patient remains fit for surgery.^{3,34} When there are no risk factors for malignancy and the undefined cysts measure ≥ 15 mm, they should be followed up at 6-month intervals for the first year and annually thereafter.^{3,21}

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Your pancreatic cystic neoplasms briefing

UEG Week

- 'Cystic pancreatic lesions' session at UEG Week 2018 [<https://www.ueg.eu/education/session-files/?session=1954&conference=153>].
- 'From guidelines to clinical practice: Cystic pancreatic lesions - differential diagnosis and management' session at UEG Week 2018 [<https://www.ueg.eu/education/session-files/?session=2051&conference=153>].
- 'New insights in the diagnosis of cystic pancreatic lesions' session at UEG Week 2018 [<https://www.ueg.eu/education/session-files/?session=2058&conference=153>].
- 'Pancreatic cystic tumours' presentation at 25th UEG week 2017 [<https://www.ueg.eu/education/document/pancreatic-cystic-tumours/155803/>] also available translated into Spanish [<https://www.ueg.eu/education/document/pancreatic-cystic-tumours-spanish-translation/171514/>].
- 'Rising Star: Pancreatic cystic neoplasias: Diagnostic approach and when to resect?' presentation at 25th UEG Week 2017 [<https://www.ueg.eu/education/document/rising-star-pancreatic-cystic-neoplasias-diagnostic-approach-and-when-to-resect/155667/>].

Society Conferences

- 'Management of cystic lesions of the pancreas' presentation at 11th EDS Postgraduate Course, Budapest 2017 [<https://www.ueg.eu/education/document/management-of-cystic-lesion-of-the-pancreas/148608/>].
- 'Pancreatic cystic lesions: When to sample them? How to follow them?' presentation from EFISDS & EPC Postgraduate Course 2015 [<https://www.ueg.eu/education/document/pancreatic-cystic-lesions-when-to-sample-them-how-to-follow-them/121062/>].
- 'IPMN - what have we learnt from the Guidelines?' presentation at EFISDS & EPC Postgraduate Course

2015 [<https://www.ueg.eu/education/document/ipmn-what-have-we-learned-from-the-guidelines/121064/>].

Standards and Guidelines

- European Study Group on Cystic Tumours of the Pancreas. European evidence-based guidelines on pancreatic cystic neoplasms. *Gut* 2018; 67: 789–804 [<https://www.ueg.eu/education/document/european-evidence-based-guidelines-on-pancreatic-cystic-neoplasms/176627/>].
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