



**The role of endoscopy in the  
diagnosis and treatment of cystic  
pancreatic neoplasms**

## CYSTIC LESIONS AND FLUID COLLECTIONS OF THE PANCREAS

Their pathology ranges from **pseudocysts** and **pancreatic necrosis** to **benign** and **malignant neoplasms**.

However, these lesions are found **incidentally in 2.5%** of patients undergoing abdominal imaging performed for unrelated reasons, and their frequency increases with age to **10%** in those **aged 70 years**<sup>3,4</sup>

## ***CYSTIC LESIONS OF THE PANCREAS***

the most common pathologic diagnoses were  
IPMNs (38%), mucinous cystic neoplasms (23%), serous  
cystic neoplasms (16%), and cystic neuroendocrine neoplasms  
(4%).

Symptomatic cystic neoplasms in this series typically  
presented with abdominal pain, pancreatitis, jaundice,  
weight loss, malabsorption, nausea, vomiting, early  
satiety, or a palpable abdominal mass.

**TABLE 2. Characteristics of pancreatic cystic lesions**

	<b>Pseudocyst</b>	<b>IPMN</b>	<b>Mucinous cystic neoplasm</b>
Clinical features	History of moderate to severe pancreatitis	History of pancreatitis, abdominal pain, or found incidentally	Usually found incidentally but can cause abdominal pain and a palpable mass if large
Morphology/ EUS findings	Anechoic, thick-walled, rare septations, regional inflammatory nodes may be seen	Dilated main pancreatic duct or side branches; may appear as a septated cyst; may have a solid component	Macrocystic, occasionally septated; peripheral calcifications, solid components and regional adenopathy when malignant
Fluid characteristics	Thin, muddy-brown	Viscous or stringy, clear	Viscous or stringy, clear
Fluid chemistries	Elevated amylase, low CEA	Elevated amylase and CEA	Elevated CEA, low amylase
Cytology	Neutrophils, macrophages, histiocytes; negative staining for mucin	Mucinous columnar cells with variable atypia; fluid stains positive for mucin	Mucinous columnar cells with variable atypia; fluid stains positive for mucin
Malignant potential	None	Yes	Yes

Data from references 9 and 17

	<b>Serous cystic neoplasm</b>	<b>Cystic endocrine neoplasm</b>	<b>Solid pseudopapillary neoplasm</b>	<b>Ductal adenocarcinoma with cystic degeneration</b>
<b>Clinical features</b>	Usually found incidentally but can cause abdominal pain and a palpable mass if large	May have clinical features of solid pancreatic endocrine neoplasm	Usually found incidentally; rarely causes abdominal discomfort	Presents with painless jaundice, abdominal/back pain or rarely pancreatitis
<b>Morphology/ EUS findings</b>	Microcystic with a "honeycomb" appearance; rarely has a macrocystic component; central calcification	Unilocular cyst occupies most of neoplasm	Solid and cystic components	Primarily solid mass with cystic spaces
<b>Fluid characteristics</b>	Thin, clear to serosanguineous	Thin, clear	Bloody + necrotic debris	Bloody ± debris
<b>Fluid chemistries</b>	Low CEA and amylase	Variable	Variable	Variable
<b>Cytology</b>	Cuboidal epithelium that stains positive for glycogen	Monomorphic endocrine tumor cells; stains positive for chromagranin and synaptophysin	Monomorphic cells with round nuclei and eosinophilic or foamy cytoplasm; stains positive for vimentin and a-1-antitrypsin	Malignant adenocarcinoma may be seen, but varying degrees of atypia may be present in the specimen
<b>Malignant potential</b>	Almost none (rare reports)	Yes	Yes	Already present

Data from references 9-11

## DIAGNOSIS BY EUS

When surgical histology is used as a reference standard, the diagnostic **accuracy** of EUS imaging ranges from **40% to 96%**

In a study among **experienced endosonographers**, the agreement whether a cyst was **neoplastic versus nonneoplastic** by EUS morphologic criteria was **fair (K Z 0.24)**, with **moderate agreement** for **serous cystic neoplasms (K Z 0.46)** and for **solid components (K Z 0.43)**.

Small cyst size alone does not exclude malignancy. One series of patients referred to a tertiary-care surgical practice reported that 20% of lesions 2 cm or smaller were malignant

A cystic lesion without septations or solid components within a pancreas having parenchymal features suggestive of pancreatitis (defined as calcifications, atrophy, or a change in echo texture) indicates a pseudocyst with a sensitivity of 94% and a specificity of 85%.

EUS imaging cannot reliably distinguish benign from malignant IPMNs.

A meta-analysis of 23 studies with 1373 patients found that a mural nodule, main pancreatic duct dilation, thickened septal walls, and cyst size >3 cm on radiologic or EUS imaging were independent predictors of malignant branch-duct IPMN.

Contrast-enhanced EUS,

which uses a contrast agent to assess the vascularity of

lesions, may aid in distinguishing inflammatory cysts

from cystic pancreatic neoplasms and vascular epithelial

mural nodules from nonvascular mucous in IPMNs.

# FNA

Cyst fluid sampled by EUS-guided-FNA (EUS-FNA) may be analyzed for **cytologic**, **chemical**, and/or **molecular** studies.

A prospective multicenter study demonstrated a **higher** diagnostic yield **when a solid component** was present on EUS (odds ratio 2.48; PZ.028;

A **dilated pancreatic duct** also can be safely targeted for **FNA when IPMN is suspected**

At present, the utility of FNA appears greatest in patients with **cysts** containing the imaging features most associated with malignancy at surgical resection, namely an epithelial nodule or mass lesion, **cyst size >3 cm**, or **main pancreatic duct dilation**.

# Cytology

Cytologic findings suggestive of a **pseudocyst** include **macrophages, histiocytes, and neutrophils**. The presence of **mucin** is suggestive of a **mucinous neoplasm** and is seen in **35%** or more of cases.<sup>21,26</sup> **Glycogen-rich** cuboidal cells indicate a **serous cystic neoplasm** but are present only in approximately **10%** of cases.<sup>7,2</sup>

A **cytology brush** (EchoBrush; Cook Endoscopy, Winston-Salem, NC) passed through a **19-gauge** needle was designed to **improve the diagnostic yield** of cyst fluid cytology obtained from EUS-FNA. However, use has been limited because of **concerns** regarding its **low incremental value over standard EUS-FNA** and potential increased **risk of adverse** events.<sup>57-60</sup>

# Chemistries and tumor markers

Because of the limited sensitivity of cytology, cyst fluid may be analyzed for levels of **amylase**, **lipase**, and tumor markers such as **CEA**.

A pooled analysis of 12 studies including 450 patients found that **amylase levels <250 U/L** virtually **excluded (specificity 98%)** the lesion as a **pseudocyst**.

A prospective, multicenter study of 112 pancreatic cysts diagnosed by surgical resection or biopsy found an optimal **CEA cutoff of 192 ng/mL** for differentiating **mucinous from nonmucinous** cysts,

## Cyst fluid DNA and molecular analysis

An **initial** study evaluated the role of molecular analysis in 113 patients and found that detection of a **K-ras** mutation was strongly associated with **mucinous cysts** and that a combined K-ras and allelic loss showed a specificity of 96% for malignancy.

**Subsequent studies**, however, found **poor agreement** between cyst fluid **CEA** levels and molecular analysis in diagnosing **mucinous** cysts,<sup>66</sup> with comparable sensitivities and diagnostic accuracies.<sup>66,67</sup> The **combination of CEA and DNA molecular analysis** improved diagnostic accuracy compared to either test alone.<sup>66,6</sup>

## Adverse events from EUS

In a systematic review of 51 studies, adverse events specific to EUS-FNA of pancreatic cystic lesions occurred in 2.7% of 909 patients

The most common adverse events include abdominal pain,<sup>77-79</sup> pancreatitis,<sup>76,77,79</sup> and intracystic hemorrhage.

current ASGE guidelines suggest administration of antibiotics for 3 to 5 days after EUS FNA of a pancreatic cystic lesion.

## Endoscopic treatment of cystic lesions

Recently, endoscopic cyst ablation with ethanol alone or in combination with paclitaxel for suspected pancreatic cystic neoplasms has been proposed as an alternative to surgery

Cysts selected for ablation have typically been less than 3 to 4 cm in size, unilocular or oligolocular (<3-6 locules), and without evidence of communication with the MPD.

Overall reported rates of cyst resolution range from 33% to 79%, with increased efficacy observed with smaller initial cyst volumes, multiple ethanol ablations, or ethanol and/or paclitaxel combination therapy.

## Recommendations

1. We recommend EUS-FNA of any pancreatic cystic lesion over 3 cm in diameter or when cross-sectional or EUS imaging confirms an epithelial nodule, dilated main pancreatic duct, or suspicious mass lesion
2. We suggest that EUS-FNA is optional in asymptomatic patients in whom cross-sectional imaging demonstrates a cyst <3 cm and without either a mass and/or epithelial nodule or associated dilated main pancreatic duct

3. We recommend initial testing of aspirated pancreatic cyst fluid for CEA, amylase, and cytology.
4. We suggest that molecular testing of the cyst be considered when initial ancillary testing of cytology and CEA is inconclusive and when test results may alter management.
5. We suggest administration of prophylactic antibiotics for patients undergoing EUS-FNA for the evaluation of cystic pancreatic neoplasms
6. We suggest that ERCP, pancreatoscopy, and intraductal US may be helpful in the diagnosis and characterization of suspected main duct IPMNs

