



Pancreatic cysts

Yonela Qubekile

Inkosi Albert Luthuli Central Hospital

24 July 2023



Pancreatic Cysts

- Known precursor lesions for pancreatic adenocarcinoma but only some are premalignant ¹
- More than 70% are detected incidentally on cross sectional imaging ²
- Pancreatic cysts are being diagnosed with increased frequency
- Prevalence of PC varies widely and ranges from 3 – 20 % depending on the imaging modality & population studied
- Discovery of pancreatic cysts imposes clinical surveillance and treatment dilemma
 - What is the risk of malignancy?
 - How morbid is the invasive management ?
 - Observe or operate ?

1.Singh et al . Diagnostics 2023

2.Ross et al. Therapeutic advances in Gastrointestinal Endoscopy 2021

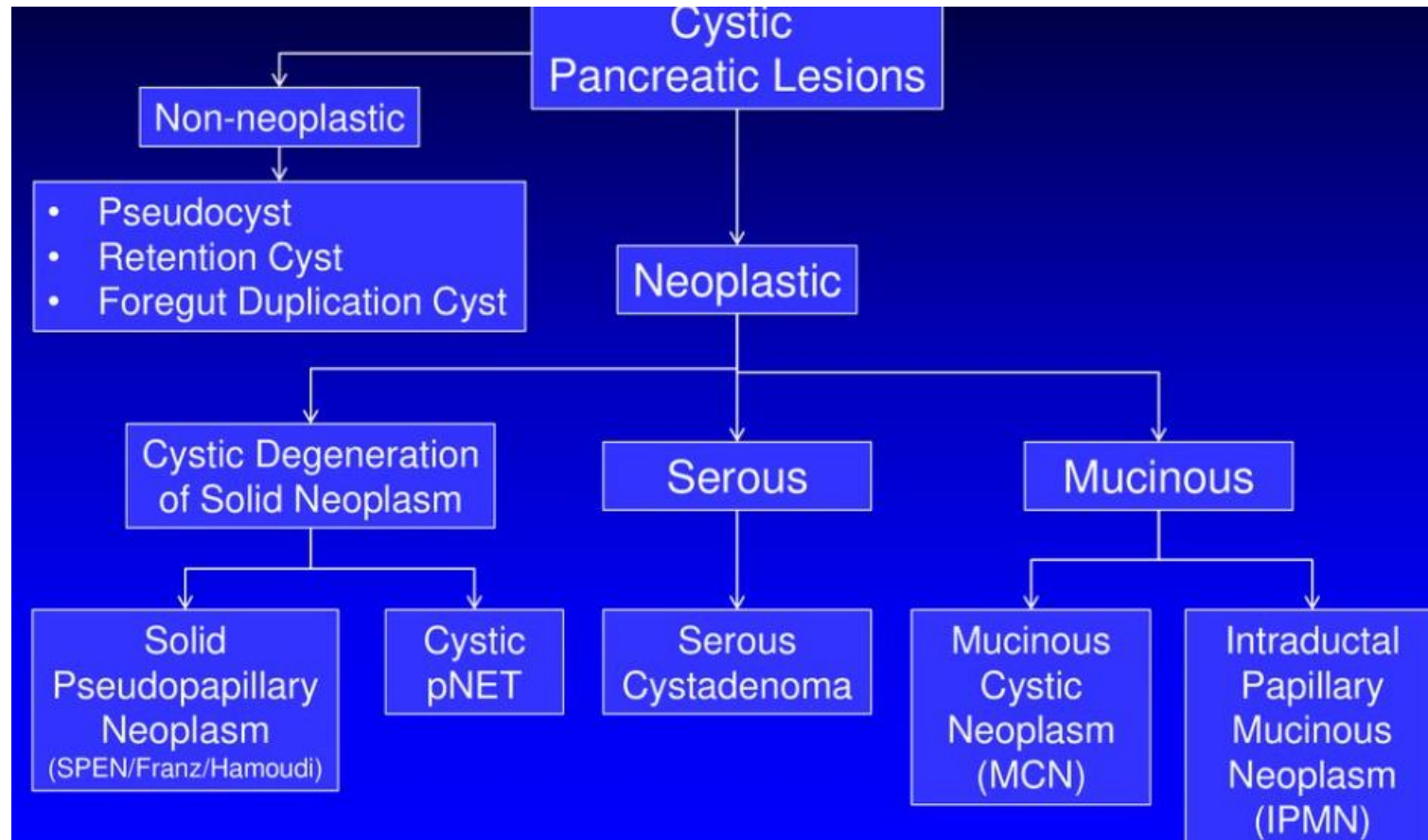
Outline

- Types of pancreatic cysts
- Imaging in PCN
- Tests Performed on cyst fluid
- Novel diagnostic methods
- Guidelines
- Cases
- Conclusion

Classification

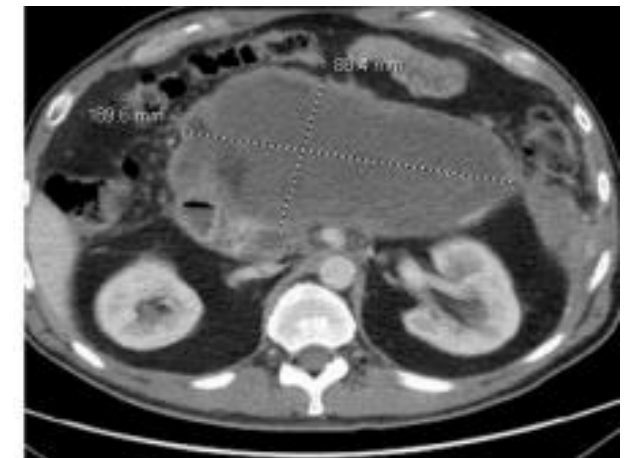
No Malignant Potential	Malignant Potential	Malignant
Pseudocyst	Intraductal papillary mucinous neoplasm	Cystic ductal adenocarcinoma
Lymphoepithelial cyst	Mucinous cystic neoplasm	Cystic neuroendocrine tumor
Retention cyst	Intraductal tubular carcinoma	Solid pseudopapillary neoplasm
Congenital cyst		Cystic pancreatoblastoma
Endometrial cyst		Cystic acinar cystadenocarcinoma
Cystic lymphangioma		Mature cystic teratoma
Cavernous hemangioma		
Serous cystic adenoma*		

Classification



Pseudocyst

- Occurs as a complication of acute pancreatitis or chronic pancreatitis
- If diagnosis unclear – EUS: fluid sampling: high fluid amylase and a low fluid CEA level < 192ng/ml
- Collection of debris, inflammatory cells & blood with thick fibrous wall
- Not lined by true epithelium
- No malignant risk therefore requires no surveillance



Solid pseudopapillary neoplasm (SPN)

- Very uncommon
 - Seen in women in their twenties
 - Patients present with abdominal mass or abdominal pain
- Imaging characteristics
 - Solid & cystic, large , well demarcated
 - Can occur anywhere in the pancreas but commonly in the tail
 - No communication with main pancreatic duct
- Cystic fluid features
 - Serous fluid (Low CEA)
 - Low amylase
- Low grade malignant risk – surgical resection is recommended (infrequently metastatic- to liver and peritoneal deposits may be seen in 5-15% cases)
- Long term prognosis is excellent



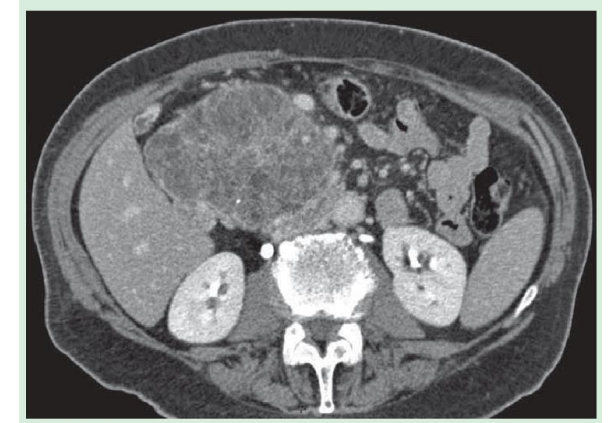
Cystic pancreatic neuroendocrine tumours (cNET)

- Up to 15% of pancreatic neuroendocrine tumours are cystic
- Arise in 5th – 6th decade
- Imaging features
 - Located in the head of pancreas with a good blood supply
 - Solid rim of arterial enhancement on CT
 - No communication with pancreatic duct
 - Focal
- Cystic Fluid features
 - Serous – low CEA
 - Low amylase
- Asymptomatic cNET < 2cm are observed (less aggressive than solid NET)
- Up to 25% are associated with MEN type 1
- Majority are non-functional



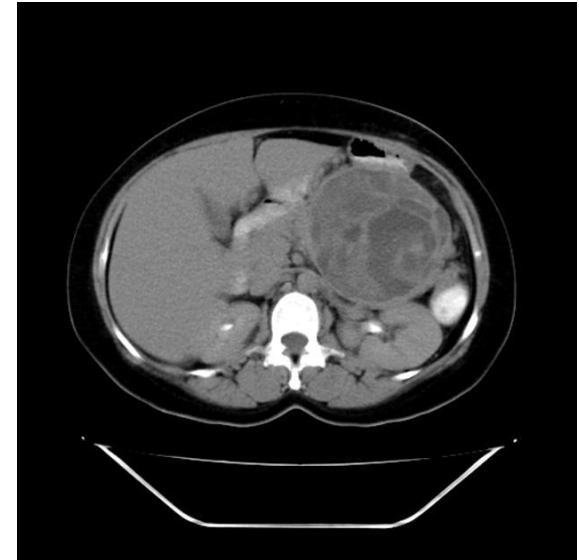
Serous Cystic Neoplasm (Serous Cystadenoma)

- 10-15% of all cystic neoplasms
- Predilection for women < 55yrs
- 80% in HOP, 80% asymptomatic
- Imaging characteristics
 - Microcystic/honeycomb & loculated, enhancing septa
 - No connection with pancreatic duct
- Cystic fluid features
 - Thin serous fluid , CEA is low (lined by cuboidal epithelium)
 - Fluid amylase is low
- Low malignant risk (5% aggressive)
- Can grow and become symptomatic – pancreatitis, abdominal pain, biliary obstruction –requiring surgical intervention



Mucinous cystic neoplasm (MCN)

- Relatively uncommon
- 95% women, mean age 48yrs
- Present with abdominal pain, weight loss, acute pancreatitis
- Imaging characteristics
 - Located in body & tail in 90-95% cases
 - No communication with pancreatic duct
 - Macrocystic, well demarcated
- Cystic fluid features
 - Mucinous - high CEA
 - Tall columnar epithelium surrounded by an ovarian-type stroma
 - Low amylase
- Risk of malignant transformation – (debated) malignant 4-12%, high grade dysplasia 6-13%
- All should be resected

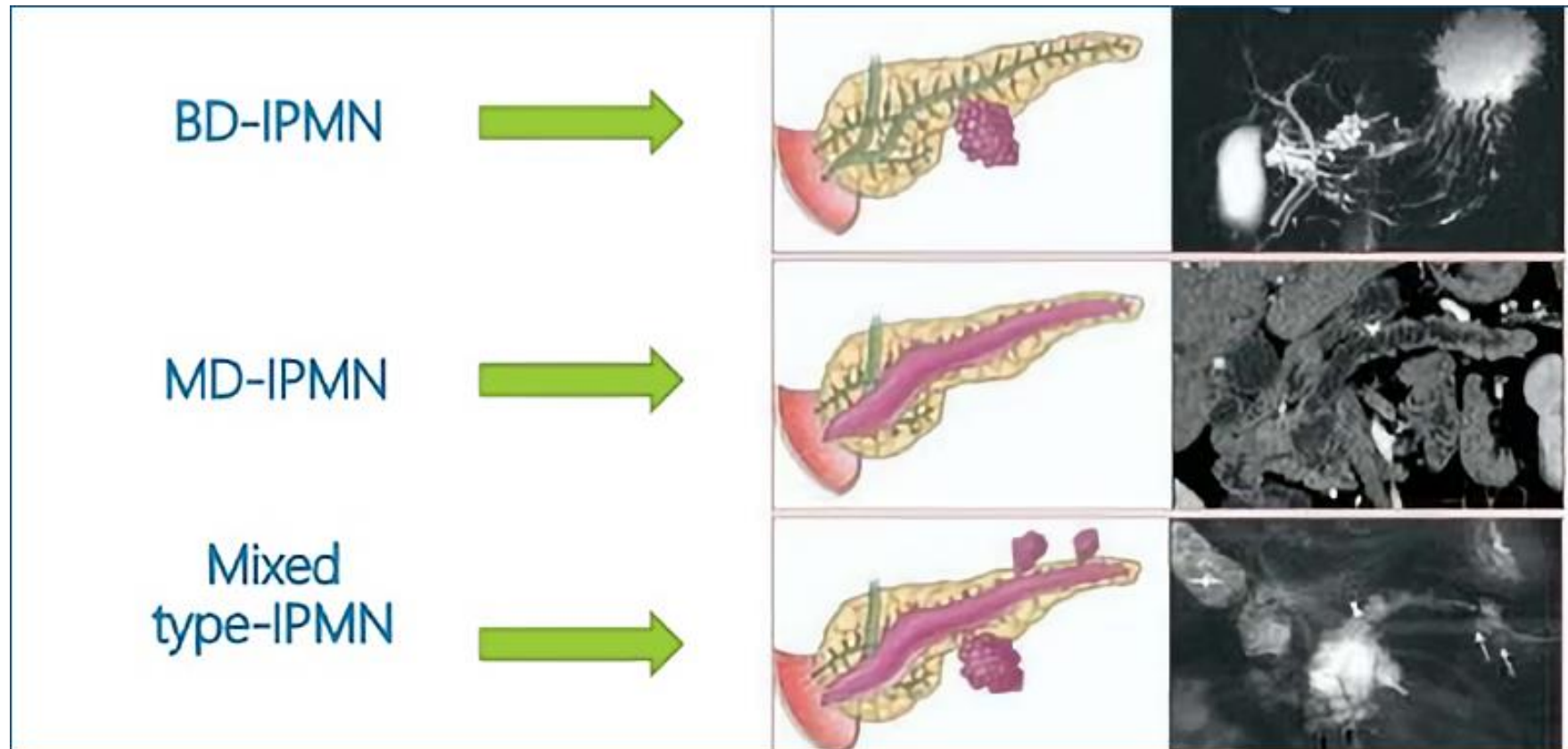


Intraductal papillary mucinous neoplasms (IPMNs)

- The most common type of MCN
- Occurs in both men & women with equal frequency
- Found in 5th – 7th decade
- Imaging characteristics
 - Occurs in head of pancreas
 - Ductal dilatation often present
 - Often multifocal, macrocystic
 - Communicates with pancreatic duct
- Cystic fluid features
 - Mucinous – high CEA
 - High amylase
- All IPMNs have malignant risk which varies based on duct involved, IPMN size, growth rate, distribution of PC

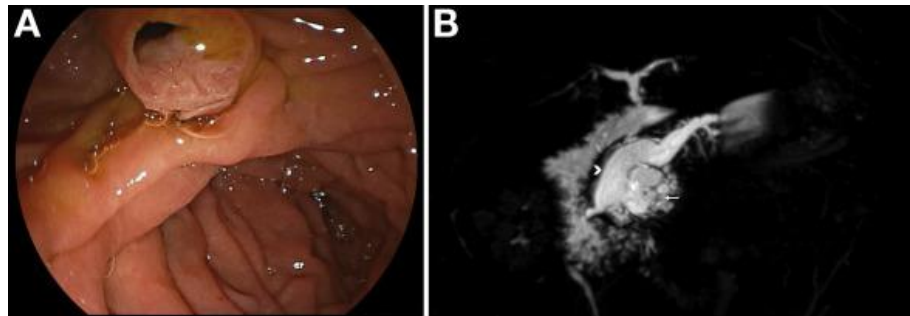
IPMNs

Classified by Relationship to Pancreatic Duct



Main Duct IPMN

- Have the highest risk of malignancy
 - Mean frequency for malignancy 61.6%
 - No consistent predictors for malignancy
 - Constitute up to 15-21% IPMNs
- Secrete thick mucous into PD → focal/segmental dilation of MPD



- MD-IPMN with dilation of PD ≥ 10 mm should be referred for surgery
- MD-IPMN with dilation of PD 5 - 9.9mm should be assessed with EUS surgery considered if high risk features

IPMNs

- BD-IPMN – most common type
 - Mean rate malignancy 25.5%
- Management of BD-IPMN is the major focus of multiple guidelines
- MT-IPMN carries a risk of malignant transformation that's comparable to MD-IPMN- resections advised in patients fit for surgery



Cross sectional imaging

Pancreas Protocol CT

- Non-invasive
- Fast
- Relatively inexpensive
- Extremely accurate in demonstrating defining characteristics
- Limitations
 - Involves radiation
 - Solid component

MRI with MRCP

- Non-invasive
- Extremely accurate in detecting high risk morphological features – mural nodule, septal thickening & cyst communication with MPD
- Sensitive in determining the solid component
- Can differentiate non-mucinous from mucinous cysts
- Limitations
 - Less readily available than CT
 - Relatively expensive

- **High risk features for malignancy**

- MPD dilation \geq 10mm
- A cyst or presence of an enhancing solid component
- Jaundice

- **Worrisome features**

- Cyst size \geq 3cm
- Septal wall thickening
- Dilated MPD 5-9mm
- A non-enhancing mural nodules
- Peri-pancreatic lymphadenopathy
- Abrupt change in MPD caliber with distal pancreatic atrophy

Endoscopic Ultrasound (EUS)

- Recommended as an adjunct to other imaging modalities
- Gold standard for identifying a solid component
- Able to obtain fluid & tissue (cyst aspiration, FNA or core biopsy)
- Role – Inconclusive imaging or worrisome or high risk features
- Limitations – more invasive, expensive for routine screening

Indications for endoscopic ultrasound	
2015 AGA	<p>≥2 high-risk features:</p> <ul style="list-style-type: none"> - Cyst size ≥3 cm - Dilated PD - Presence of a solid component
2017 International Consensus	<p>If any of the following present:</p> <ul style="list-style-type: none"> - Pancreatitis due to cyst - Cyst size ≥3 cm - Enhancing mural nodule <5 mm - Thickened/enhancing cyst walls - PD 5–9 mm - Abrupt change in diameter of PD with distal pancreatic atrophy - Lymphadenopathy - Elevated CA-19-9 - Rapid growth of cyst (>5 mm/2 years)
2018 ACG	<p>If any of the following present:</p> <ul style="list-style-type: none"> - PD ≥5 mm - IPMN or MCN ≥3 cm - Change in PD caliber with upstream atrophy - Size increase of ≥3 mm/year during surveillance - Jaundice due to cyst - Pancreatitis due to cyst - Presence of a mural nodule or solid component
2018 European	<p>Clinical or radiological features of concern for malignancy Can be alternated or done in conjunction with MRI during surveillance</p>
<p>ACG, American College of Gastroenterology; AGA, American Gastroenterological Association; CA-19-9, carbohydrate antigen 19-9; MRI, magnetic resonance imaging; PCN, pancreatic cystic neoplasm; PD, main pancreatic duct.</p>	

Cyst Aspiration & Biopsy

Cyst Aspiration

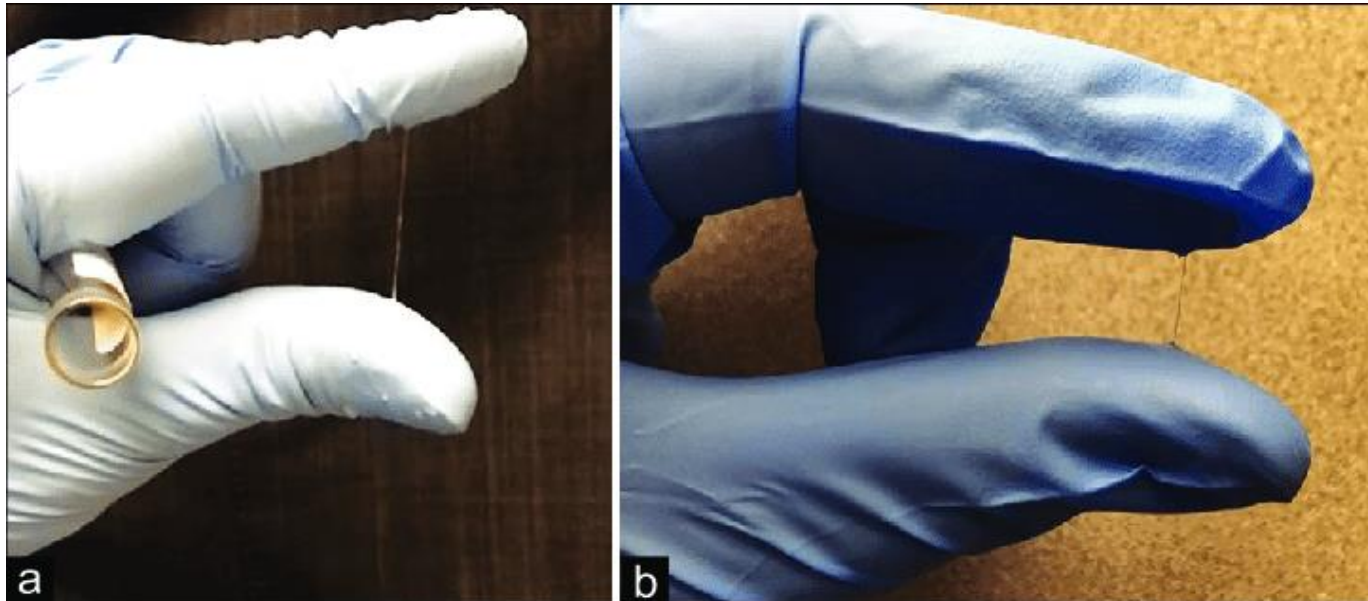
- Helpful in differentiating serous from mucinous
- Solid component
- CEA level
- Genetic analysis
- Limitations
 - Highly operator dependent
 - Often cannot obtain fluid
 - GI tract contamination

FNA or Core Biopsy

- Level of dysplasia
- Able to perform immunochemistry
- Limitations
 - Often indeterminate
 - Loss of cytoarchitecture
 - False negatives (dysplasia/cancer)

Diagnosis with EUS: Mucinous vs. Nonmucinous

EUS findings	Test characteristics
Morphology	51% accuracy
String sign $\geq 1\text{cm}$, $\geq 1\text{sec}$	95% specificity, 94% PPV



Diagnosis with EUS: Mucinous vs. Nonmucinous

EUS findings	Test characteristic
Morphology	51% accuracy
String sign $\geq 1\text{cm}$, $\geq 1\text{sec}$	95% specificity, 94% PPV
Cyst fluid cytology	63% sensitivity
Cyst wall cytology	29% increased diagnostic yield
CEA $> 192\text{ ng/mL}$	75% sensitivity, 84% specificity

Serum CA-19.9 $>37\text{ units/ml}$ associated with increased risk of malignancy – pooled sensitivity 40% pooled specificity 89%

Relative indication for surgery in the European guideline

Indication for EUS & surgery in the International consensus guidelines

Diagnosis with EUS: Other Cyst Fluid Markers

Cyst Fluid Markers		Sensitivity	Specificity
CEA < 5ng/mL	Serous, pseudocyst Cystic neuroendocrine	50%	95%
Amylase <250 U/L	Excludes pseudocyst	44%	98%
KRAS + allelic loss	Malignancy	25 – 37%	94-96%
GNAS	IPMN	-	Highly specific for IPMN
Glucose <50mg/dl	Mucinous cyst	95%	57%

Technique of EUS FNA

- Cyst \geq 1cm
- 22 gauge needle
- 1 pass, drain entire cyst, then FNA collapsed cyst wall for cytology
- Target nodule/solid component with needle
- Assess for string sign, cyst fluid CEA, amylase, potentially KRAS, GNAS
- Prophylactic antibiotics – single dose
- Safe – low risk 3.4% complication

Mural nodules

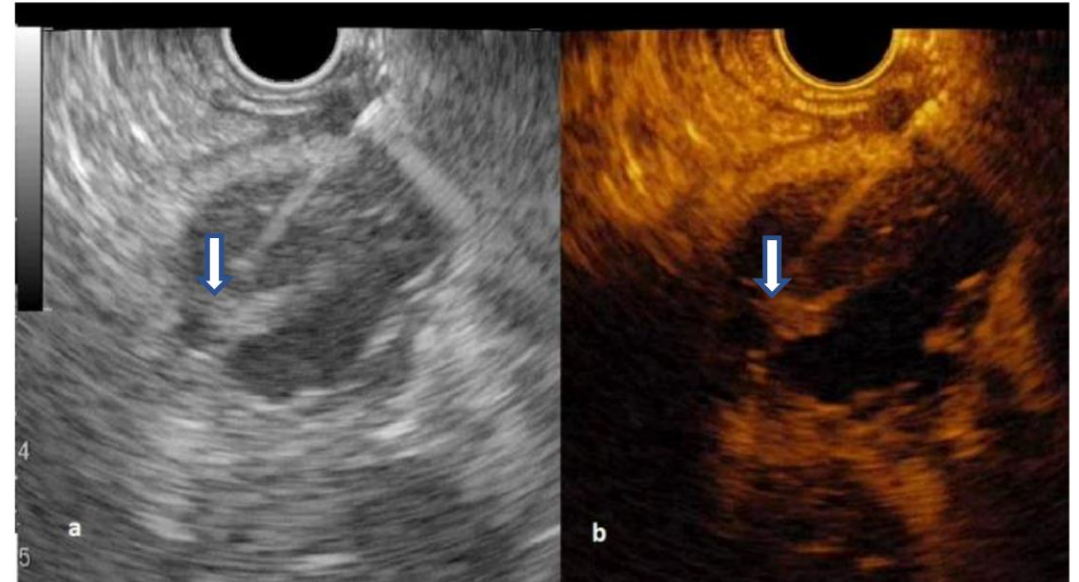
- Solid component in the wall of the pancreatic cyst
- Associated with increased risk of malignancy
 - A large metanalysis by Anand et al. found the presence of mural nodule had an OR 9.3 (5.3 – 16.1) for developing malignancy¹
 - A systemic review showed OR 7.73 (3.38 – 17.67) for developing malignancy²
 - Another metanalysis found the presence of mural nodule had an OR 6.0 (4.1-8.8) for malignancy³
- How good are we at detecting mural nodules?
 - Not good 40 - 60%
 - EUS sensitivity 75%, specificity 89%
 - CT sensitivity 47%, specificity 89%



1. Anand et al. *Clin Gastroenterol Hepatol* 2013
2. Kim et al. *Annals of surgery* 2014
3. Sherman et al. *Gastroenterology* 2015
Zhong et al. *Clin Gastro Hepat* 2011

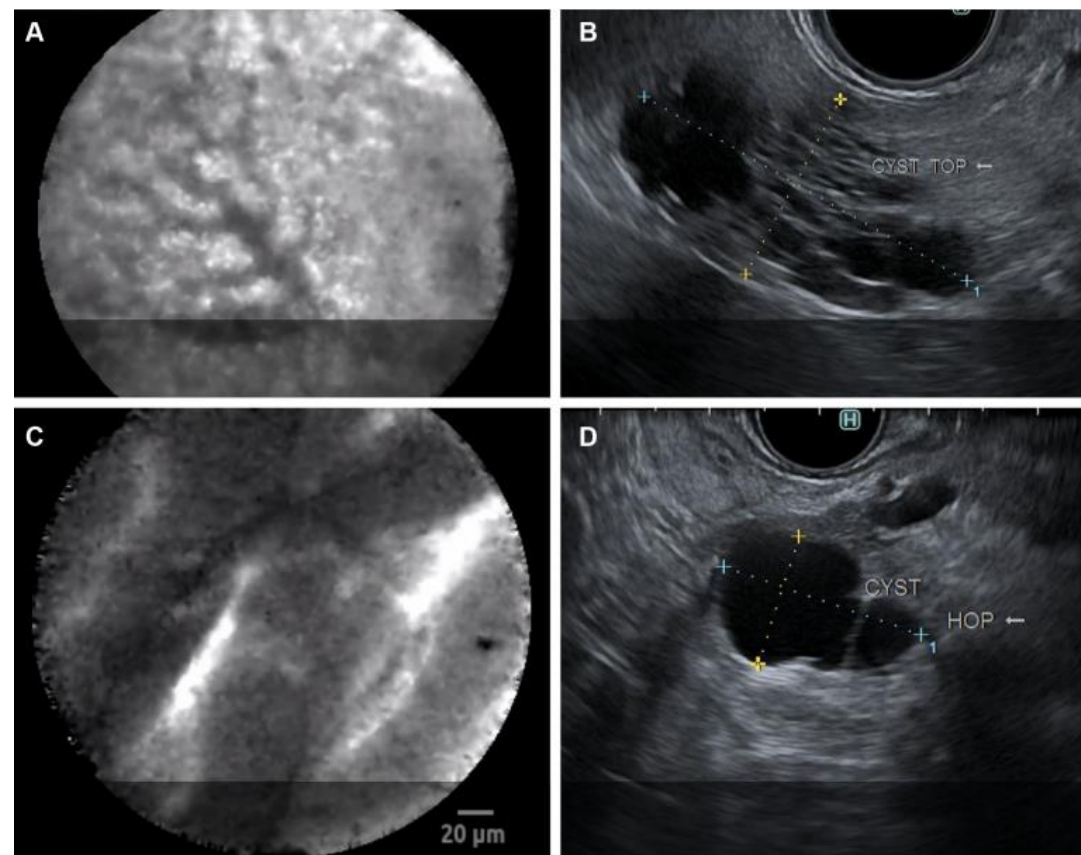
Mural Nodules: Can We Do Better?

- Contrast enhanced harmonic EUS
 - Injected contrast agent visualizes vascularity of nodules, cyst wall, septations
- Differentiates mural nodule (enhanced) from mucus (non-enhancing)
- In a meta-analysis of over 500 patients CE-EUS had high sensitivity 88% and specificity 79% in detecting mural nodules within the pancreatic cyst



Needle-based Confocal Laser Endomicroscopy

- A confocal laser endomicroscope probe is introduced through EUS directed 19-gauge needle
- Pancreatic cyst epithelium can be microscopically imaged in real time
- Can differentiate pancreatic cysts types
 - Mucinous – characterized by epithelial features with papillae & epithelial bands
 - Cystic neuroendocrine lesions – trabecular pattern
 - SCA- fern pattern of vascularity

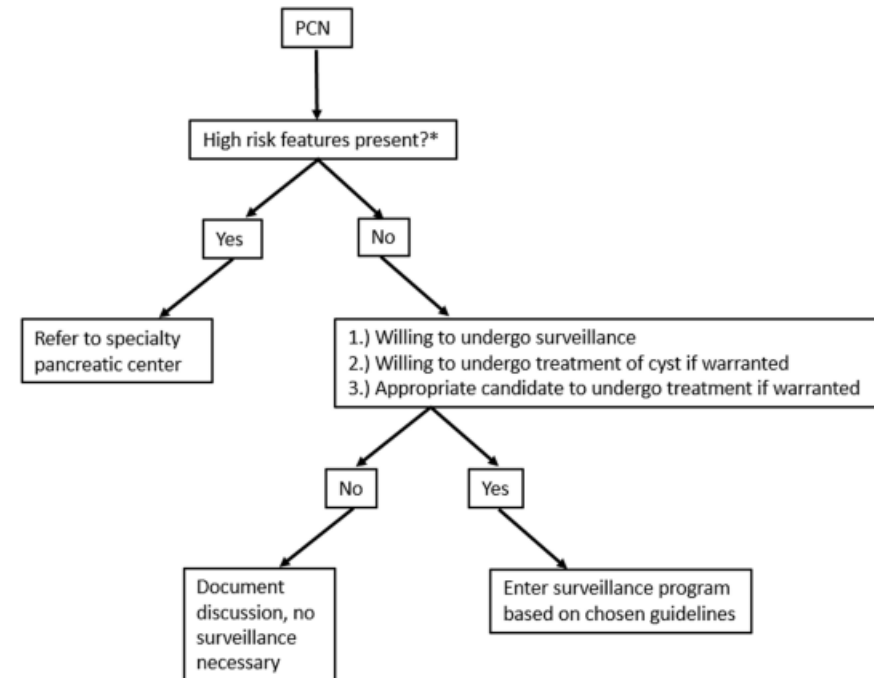


Distinguishing the cysts

Cyst Type	Age of Presentation	Gender Predisposition	Clinical Presentation	Distribution	Morphologic Features	Malignant Potential
IPMN	>65–70 years [9,10]	M > F	1/3 of patients symptomatic (epigastric pain, back pain, weight loss), acute pancreatitis, new-onset diabetes, obstructive jaundice	Head and neck > body/tail	PD dilatation, BD- and mixed IPMN multiloculated	Depends on main PD involvement. MD-IPMN and mixed-IPMN malignant in 45–60%. High-risk: main PD > 1 cm, solid component or enhancing nodule, jaundice, HGD
Mucinous cyst	<70 years	F > M	Abdominal pain, weight loss, acute pancreatitis	Body or tail	Solitary, unilocular with ovarian-like stroma, peripheral calcification, no PD dilation	Malignant 4–12%; HGD 6–13%. High-risk: >6 cm, irregular thick wall, peripheral calcification
Serous cystadenoma	<55 years	F >> M	Rarely jaundice and weight loss	3/4 in body or tail	Solitary, “Central scar”, no PD dilation	Low malignant risk, ~5% aggressive
Solid pseudopapillary neoplasm	<30 years	F > M	Jaundice and weight loss uncommon	Any location, more commonly tail	Solitary, solid component, mural nodule, peripheral calcification	Low-grade malignant neoplasms, infrequently metastatic

Approach to pancreatic cyst

- Prior surveillance program – discuss with patient the potential risks and benefit, as risk of tolerance varies greatly between patients
- Also consider morbidity and mortality associated with pancreatic surgery (morbidity 30-40%, mortality 4% following pancreatic surgery)
- If the patient is not a candidate for or unwilling to undergo surgery or chemotherapy or if they have a limited life expectancy – surveillance is not indicated as it would not alter management
- Psychological burden of undergoing routine surveillance



Guidelines

- International Consensus Guideline -Sendai (2006), Fukuoka (2012), Revised Fukuoka (2017)
- European Experts Consensus Statement – 2013
- American Gastroenterology Association (AGA) 2015
- ASGE (regarding endoscopic role) 2016
- American College of Gastroenterology 2018
- European Guidelines 2018

Indications for surgical resection

2015 AGA	Positive cytology on EUS-guided FNA; both a solid component and dilated PD
2017 International Consensus	Obstructive jaundice with PCN in head of pancreas; enhanced mural nodule ≥ 5 mm; PD ≥ 10 mm; MD-IPMN; cytology suspicious or positive for malignancy
2018 ACG	All MD-IPMNs; cytology with high-grade dysplasia or malignancy; mural nodule; concerning features on EUS
2018 European	<i>Absolute indications:</i> Cytology suspicious or positive for malignancy or high-grade dysplasia; solid component; obstructive jaundice with PCN in head of pancreas; enhancing mural nodule > 5 mm; PD ≥ 10 mm; symptoms due to PCN <i>Relative indications:</i> PCN growth rate ≥ 5 mm/year; elevated CA-19-9 level; PD 5–9.9 mm; PCN size ≥ 40 mm; new-onset diabetes mellitus; acute pancreatitis (due to PCN); enhancing mural nodule < 5 mm

ACG, American College of Gastroenterology; AGA, American Gastroenterological Association; BD-IPMN, branch duct intraductal papillary mucinous neoplasm; CA-19-9 carbohydrate antigen 19-9; EUS, endoscopic ultrasound; FNA, fine needle aspiration; IPMN, intraductal papillary mucinous neoplasm; MCN, mucinous cystic neoplasm; PCN, pancreatic cystic neoplasm; PD, main pancreatic duct.

Management of mucinous cysts neoplasms of the pancreas

	2015 AGA	2017 International Consensus	2018 ACG	2018 European
Management of MCN	Same as management for IPMN	Surgical resection for all surgically fit patients	Same as management for IPMN	Surgical resection if any of the following: size ≥ 4 cm, symptomatic, have high-risk features (same as those for IPMNs) If size < 3 cm, surveillance (same as IPMNs)

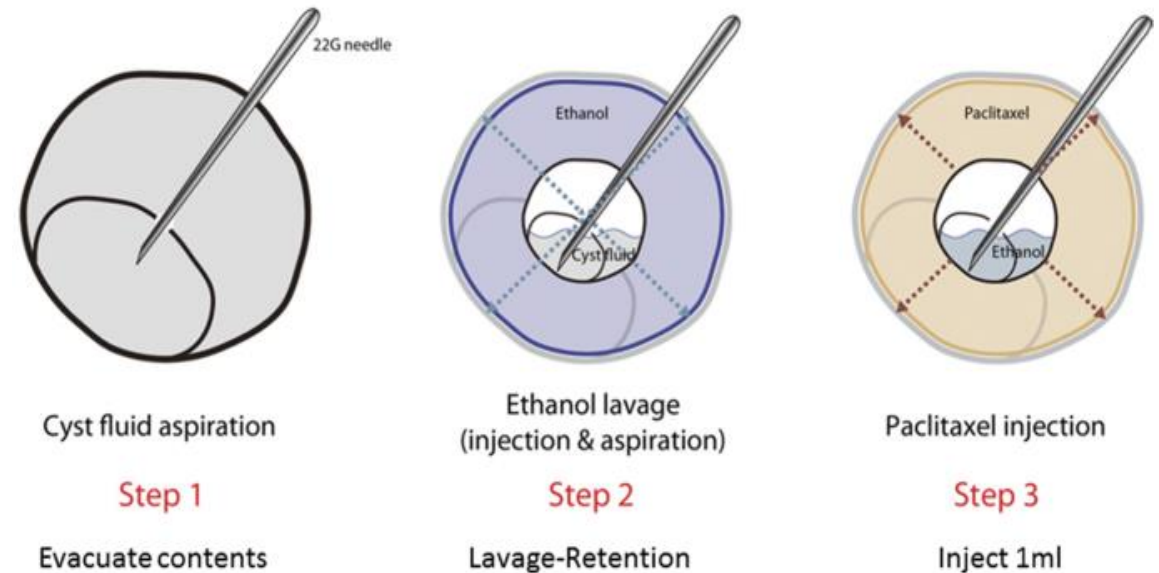
Cyst size	2015 AGA	2017 International Consensus	2018 ACG	2018 European
<1 cm	If no solid component and no dilated PD and cyst <3 cm: MRI in 1 year then every 2 years for 5 years if no change (then can stop if no change)	MRI or CT in 6 months, then every 2–3 years if no change	MRI every 2 years × 4 years (then consider lengthening)	Year 1: MRI or EUS every 6 months (in addition to serum CA-19-9 level and clinical evaluation) After Year 1: MRI and/or EUS every 1 year (in addition to serum CA-19-9 level and clinical evaluation) ≥4 cm: resection
1–2 cm		MRI or CT: Year 1: every 6 months Years 2–3: yearly After 3 years: every 2 years if no change	MRI every 1 year × 3 years, then every 2 years × 4 years (then considering lengthening)	
2–3 cm		EUS in 3–6 months, then every year (can alternate with MRI)	MRI or EUS every 6–12 months × 3 years, then MRI every 1 year × 4 years (then lengthen)	
>3 cm		Alternate EUS and MRI every 3–6 months	Refer to multidisciplinary group and alternate EUS and MRI every 6 months × 3 years, then every 1 year × 4 years (then consider lengthening)	

ACG, American College of Gastroenterology; AGA, American Gastroenterological Association; CA-19-9, carbohydrate antigen 19-9; EUS, endoscopic ultrasound; PD, pancreatic duct.

EUS Guided Cyst Ablation

- EUS –guided pancreatic cyst ablation
- Injecting ethanol or anti-tumor agents or radiofrequency ablation- in patients unable or unwilling to undergo surgery

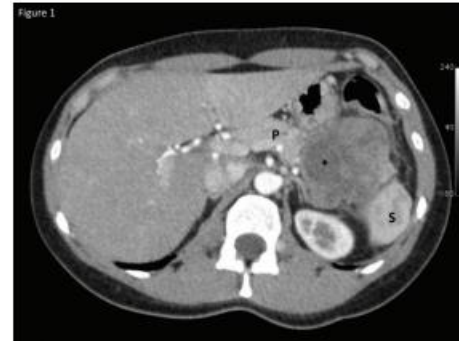
EUS Guided Cyst Ablation Technique



Solid Pseudopapillary Neoplasms of the Pancreas: A Report of Two Cases

Dilip Dan, Rakesh Rambally, Shamir O. Cawich, Ravi Maharaj, and Vijay Naraynsingh

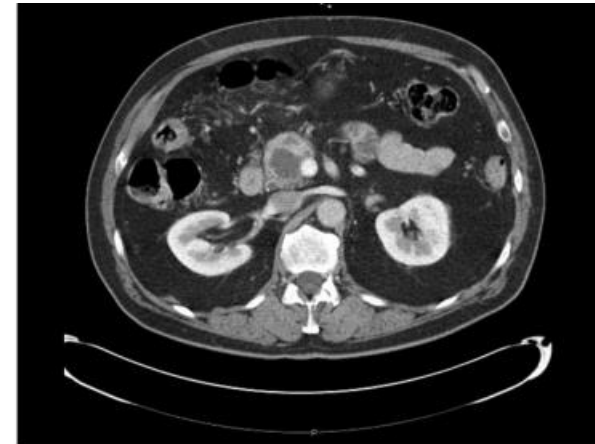
- 35 year old woman p/w vague epigastric discomfort – 18months
- U/S abdo- ? Pancreatic tumor
- CT- scan- well-circumscribed lesion in the pancreatic tail, 6cm, peripheral enhancement & central area of cystic degeneration
- Diagnosis of Solid psuedopapillary neoplasm
- Distal pancreatectomy performed



Cystic neuroendocrine tumor in the pancreas detected by endoscopic ultrasound and fine-needle aspiration: a case report

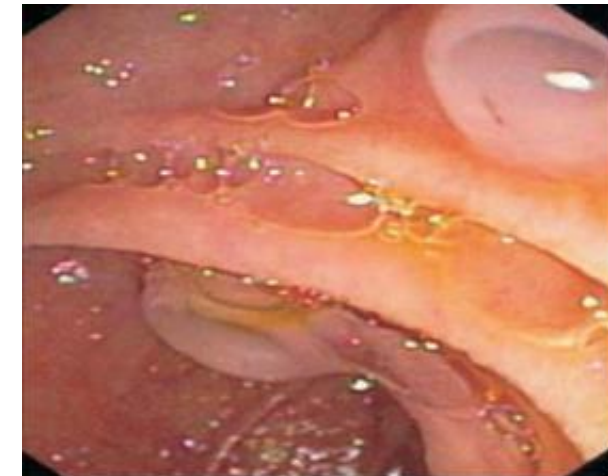
Henrik Thorlacius^{1*}, Evangelos Kalaitzakis², Gabriele Wurm Johansson², Otto Ljungberg³, Olle Ekberg⁴ and Ervin Toth²

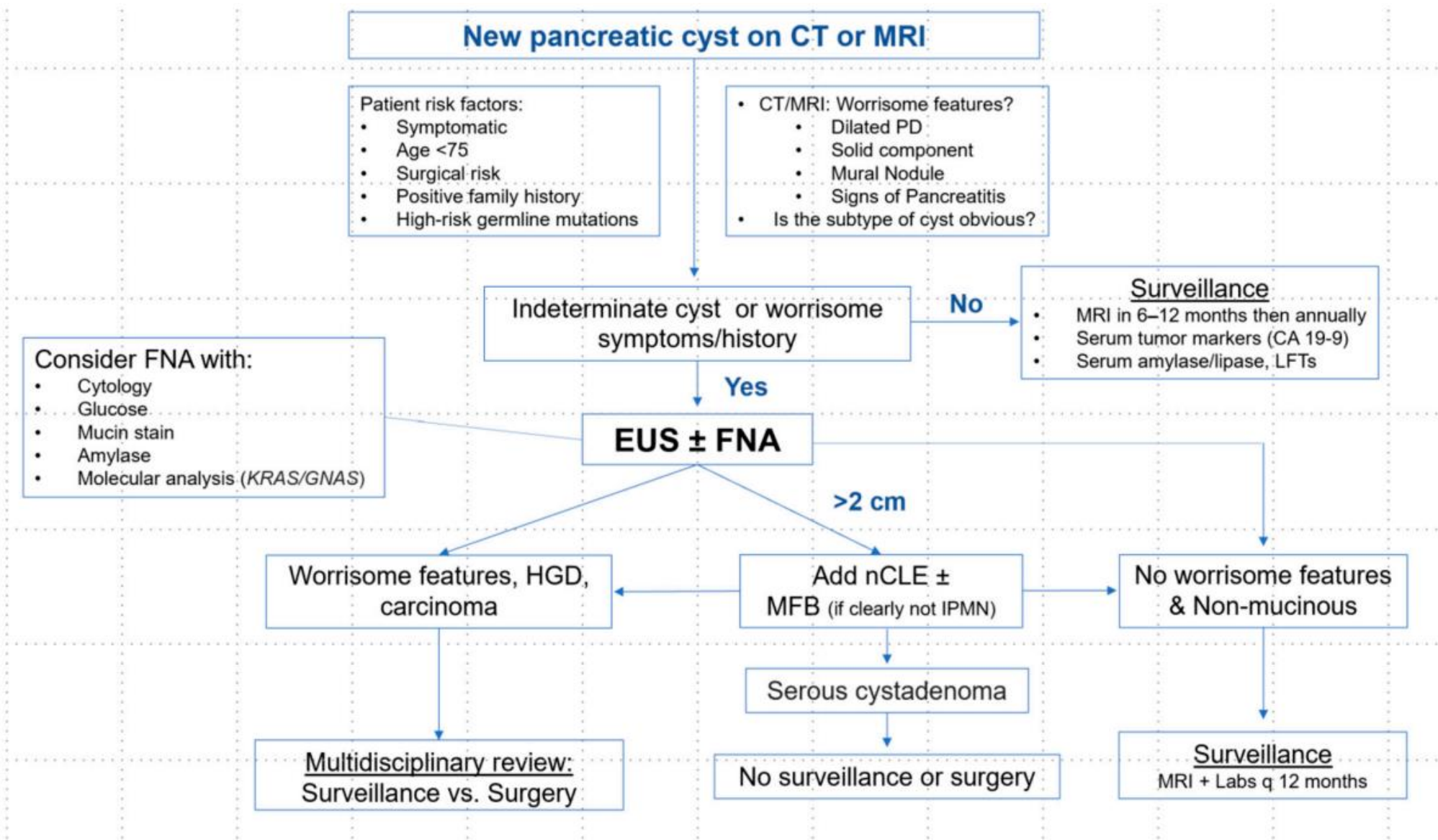
- 78 year old man p/w epigastric pain
- Laboratory test were normal
- Transabdominal U/S – suspicious lesion –HOP
- Contrasted CT- abdo- 4x5cm cystic mass, no PD dilatation
- EUS- hypoechoic lesion 42x 47mm, FNA done
- Cystic fluid- low viscosity, normal CEA and amylase
- Cytology – cohesive plasmocytoid cells staining positively for synatophysin & chromograninA



Intraductal papillary mucinous neoplasm of the pancreas

- 53 year old woman p/w 2 month hx of recurrent epigastric pain, radiating to the back
- Relieved by oral analgesics, no fever or weight loss
- No history of alcohol/smoking
- Lab: Hb 10.4g/dL, serum amylase normal, serum ALP 468IU (40- 125), Ca19. 9- 307 (<33)
- Fluid from the pancreatic duct showed atypical cells
- She underwent Whipple's resection
- Histopathology examination revealed an IPMN of pancreas (main duct type) with moderate dysplasia
- The resection margin and regional lymph nodes were free of tumor





Conclusion

- Significant variability exists in the malignant potential and management recommendations of pancreatic cysts
- The key is to distinguish mucinous vs non-mucinous
- Mucinous neoplasms meeting the guideline criteria should be resected
- Presumed IPMN must be followed up
- Patients with pancreatic cysts benefit from a multidisciplinary team approach, which includes gastroenterologists, pancreatic surgeons, radiologists, cytopathologists and pathologists
- Novel EUS- guided imaging and tissue sampling modalities may allow for more definitive diagnosis avoiding further surveillance for benign cysts