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Gastroenterology Foundation of sub Saharan Africa

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GI HEPATOLOGY ECHO OF SUB-SAHARAN AFRICA
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PANCREATIC CYSTS

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INTRODUCTION

- Once considered rare and of uncertain clinical significance (NEJM 1934)
- Prevalence
  - 2% -15% from imaging studies
  - Up to 50% from some autopsy series
- Incidence on the rise
  - Even with consideration of increased cross-section imaging usage
  - Increases with age

INTRODUCTION

- Overal risk of malignancy could be 0.5%-1.5%
  - Annual risk of progression of 0.5%
- 15% of pancreatic adenocarcinomas arise from mucinous cysts
- Identification of high risk cysts offers a window for prevention/early detection of cancer
  - This is challenging since benign and low risk cysts are much more common

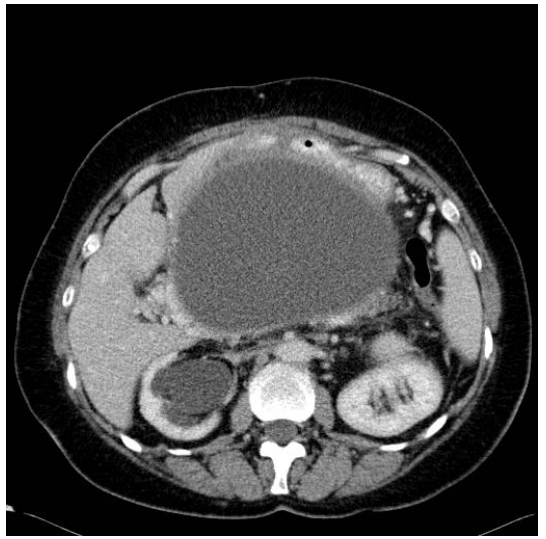
DIAGNOSIS OF PANCREATIC CYSTS

- There are >20 types of epithelial and non-epithelial cysts
- 6 most common histological categories
  - Pseudocysts
  - Serous cystadenoma
  - Intraductal papillary mucinous neoplasms (IPMN)
  - Mucinous cystic neoplasms (CMN)
  - Solid pseudopapillary neoplams
  - Cystic pancreatic neuroendocrine tumours

PANCREATIC PSEUDOCYSTS

- Post AP/CP
  - Without history of pancreatitis, diagnosis should be made with caution
  - If seen with ongoing pancreatitis, could be a cause not a complication
- Single or multiple unilocular cysts
  - Contain pancreatic fluid,
- Not lined by true epithelium
- Usually connected to the PD (70%)
  - Could be challenging on CSI to confirm that

PSEUDOCYSTS



Jones J. *Radiopedia* 2009

- Symptoms:
  - Abdominal pain
  - Palpable mass
  - Nausea/vomiting
  - Jaundice
- Diagnosis: imaging
  - USS, EUS, CT,MRI
- Complications: in 20-40%
  - Compression of duodenum/stomach/peripancreatic vessels
  - Infection
  - Haemorrhage
  - Fistula formation

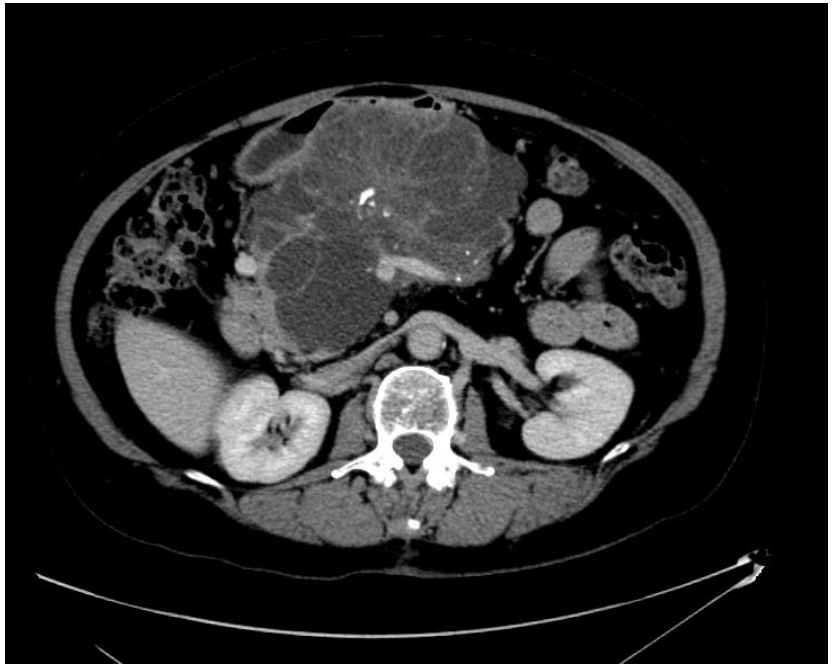
TREATMENT

- Indications
  - Symptomatic
  - Complicated
  - Rapidly growing
- Options
  - Endoscopic: cystogastrostomy/cystoduodenostomy/transpapillary
  - Surgical
  - Percutaneous: not really encouraged, due to risk of recurrence and formation of fistulae

SEROUS CYSTADENOMA

- Benign, slow growing lesions
- Women in 5th-7th decades of life, mean age of 62
- Some association with VHL disease
- Most cases are asymptomatic- incidental finding on CSI
- Can present with abdominal pain, discomfort, palpable mass

IMAGES



Radswiki T. *Radiopaedia.org*. 2010

Di Muzio B. *Radiopaedia.org.* 2013

Gardner TB. et al
Gastroenterology 2024

MANAGEMENT

- Observation can be safely done if asymptomatic
  - Risk of continued growth- compression, haemorrhage
- Rates of growth?
  - Slow: 1mm/yr
  - Rapid: 5mm/yr
- Surgical consideration
  - New onset/worsening symptoms
  - Rapid growth
  - Concern for serous cystadenocarcinoma: few cases in literature described

MUCINOUS CYSTIC NEOPLASMS

- Less common type of mucinous cysts
  - Prevalence: ½ of IPMNs
- Female to male ratio: 20 to 1
  - Women in 4th to 6th decades of life, mean age of 50
- 95% in the body and tail of pancreas
- Appear as solitary, uni/multilocular lesions with a thick wall
  - Surrounded by ovarian-type stroma
- No connection to PD
  - Differentiates from IPMNs

MCN

- CSI: peripheral (egg shell) calcifications are diagnostic
- EUS:
  - If CSI can not confirm the diagnosis
  - Can identify septations and wall nodules better than CT/MRI
  - Allows cystic wall biopsy and fluid aspiration
- Fluid analysis:
  - Thick mucinous fluid
  - Low amylase
  - High CEA
  - Low glucose

Quingalahua E. et al. *Diagnostics* **2023**,

TREATMENT OF MCN

- Risk of neoplasia is as high as 30%
- Surgical resection advocated for all
  - Distal pancreatectomy +/- splenectomy
  - Peripancreatic LN excision
- 5yr survival for benign/borderline lesions is 100%
  - No need for long term follow up
- 5yr survival for invasive MCNs is 30-60%

GUIDELINE BASED MANAGEMENT FOR MCN

Type of Action	European Guidelines (2018) [11]	ACG Guidelines (2018) [7]	AGA Guidelines (2015) [1] [75]
Surveillance	MCN < 40 mm without risk factors and symptoms can be safely surveilled with MRI, EUS, or a combination of both every 6 months for the first year and then annually as long as they are fit for surgery.	Surveillance of surgically fit candidates with asymptomatic cysts. Patients with new-onset or worsening DM, or increase in cyst size > 3 mm/year, should undergo a short-interval MRI or EUS ± FNA.	MRI surveillance during 1st year and then every 2 years for a total of 5 years for cysts < 30 mm without solid component or dilated pancreatic duct and for cysts without concerning EUS-FNA results.
Indication for resection/referral to a multidisciplinary group [3]	MCN ≥ 40 mm, symptomatic MCN, and MCN with high risk factors, like a mural nodule, regardless of its size.	MCN > 30 mm; MCN with mural nodule or solid component; dilated pancreatic duct > 5 mm; jaundice or acute pancreatitis secondary to the cyst; significantly elevated serum CA 19-9; the presence of HGD or pancreatic cancer upon cytology.	MCN with both a solid component and a dilated pancreatic duct and/or concerning features on EUS and FNA [2].
Post-surgery surveillance	No data.	No surveillance for resected MCNs without pancreatic cancer.	No routine surveillance for cysts without HGD or malignancy at resection.

INTRADUCTAL PAPILLARY MUCINOUS NEOPLASIA

- Most common type of mucinous cystic lesions
- Equal sex distribution
- Incidental diagnosis; found in up to 10% of subjects over 70yrs
  - Peak incidence between 5th and 7th decades of life (median age 65)
- Tend to be multifocal, located throughout the pancreas
  - Arise from the ductal cells
- Types
  - Main duct
  - Branch-duct
  - Mixed

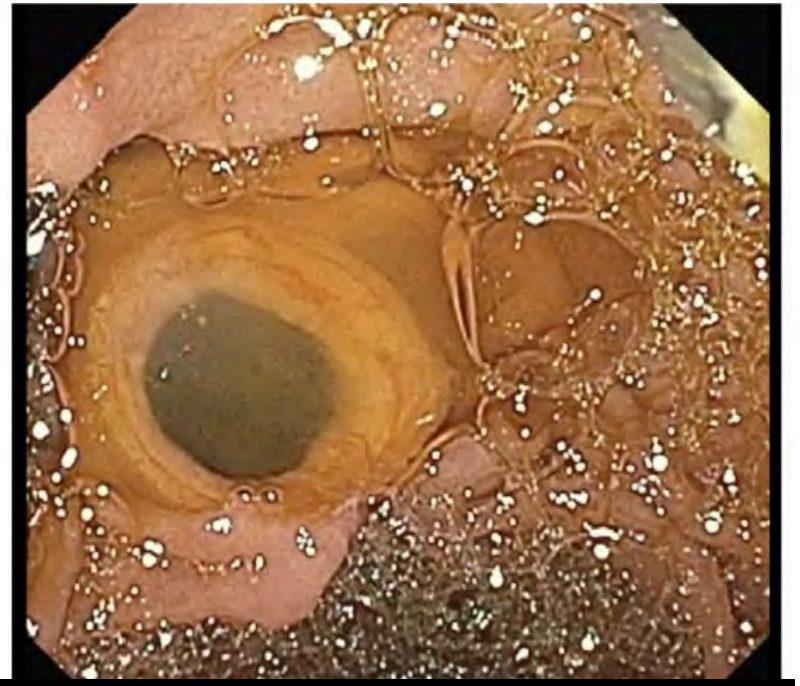
IPMNs

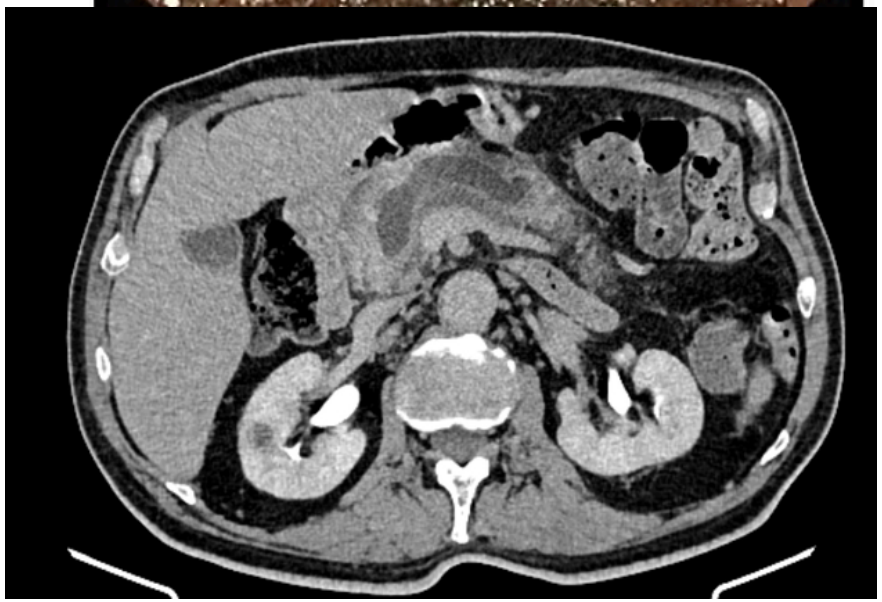
- Up to 75% of patients are asymptomatic
- Symptoms range from abdominal pain to weight loss, jaundice
- History of pancreatitis in 20%
- Some patients have active pancreatitis at time of diagnosis- up to 25%
- Histology:
  - Benign
  - Borderline
  - Malignant: could be non-invasive or invasive
- Fluid analysis: high CEA, high amylase, high viscosity, low glucose

MAIN DUCT IPMNS

- Diffuse dilatation of the main duct
  - Due to mucin hypersecretion
- Risk of maliganancy: up to 80%
- Fish mouth papilla on endoscopy- pathognomic
  - Bulging
  - Extruding mucin
- CT/MRI (+MRCP)
  - Dilated PD +/- cystic mass

Kaila V et al 2024





Elfeky M. *Radiopaedia.org*. 2018

BRANCH DUCT IPMNS

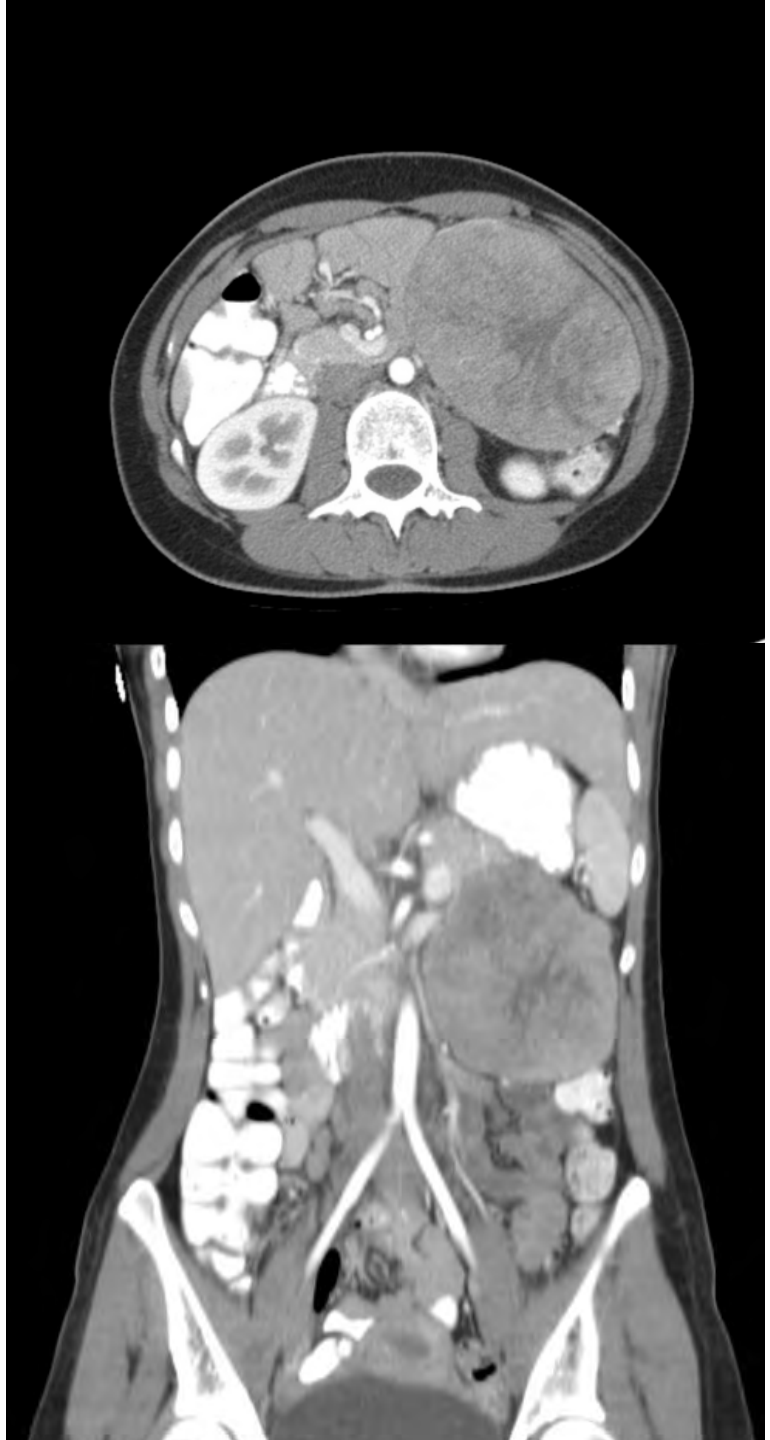
- Can be single or unlocular
- Often occur in clusters, resembling grapes
- Risk of malignancy up to 38%

TREATMENT

- Pancreatic resection
  - Pancreaticoduodenectomy is the treatment of choice in many patients due to predilection of lesions in the head of pancreas
  - Distal resection can be done if lesion in body/tail of pancreas
- 5 yr survival up to 75%
- Predictors of worse outcomes
  - Lymph node mets
  - Perineural/lymphovascular invasion
  - Positive resection margins
- Disease recurrence common even after negative margins
  - Need for follow up

SOLID PSEUDOPAPILLARY TUMOUR

- Rare, first described in 1934
- Disease of young women
  - 2nd to 3rd decades
  - Women: men=10:1
- Present with abdominal pain/palpable mass
  - 15% incidental finding
- 60% in body/tail of pancreas
- Well demarcated and heterogenous appearance
- Solid and cystic components



Glick Y. *Radiopaedia.org* 2017

SPT

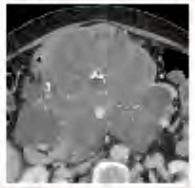
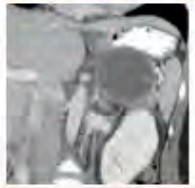
- Most demonstrate benign behaviour
- 10-20% classified as carcinoma on assessment
- 5-10% already have liver mets at diagnosis
- >90% have mutations in B-catenin gene

- Resection in the treatment of choice
  - 100% 5yr-survival with R0 resection

CYSTIC PANCREATIC NEUROENDOCRINE NEOPLASMS

- From endocrine cells
- Cystic degeneration of pNETs
- Have thick enhancing walls on radiology
- Most are sporadic and nonfunctioning
- 10% as part of MEN1
- >80% express somatostatin receptors
  - Role of octreotid scan
- Features of poor prognosis similar to solid pNETs

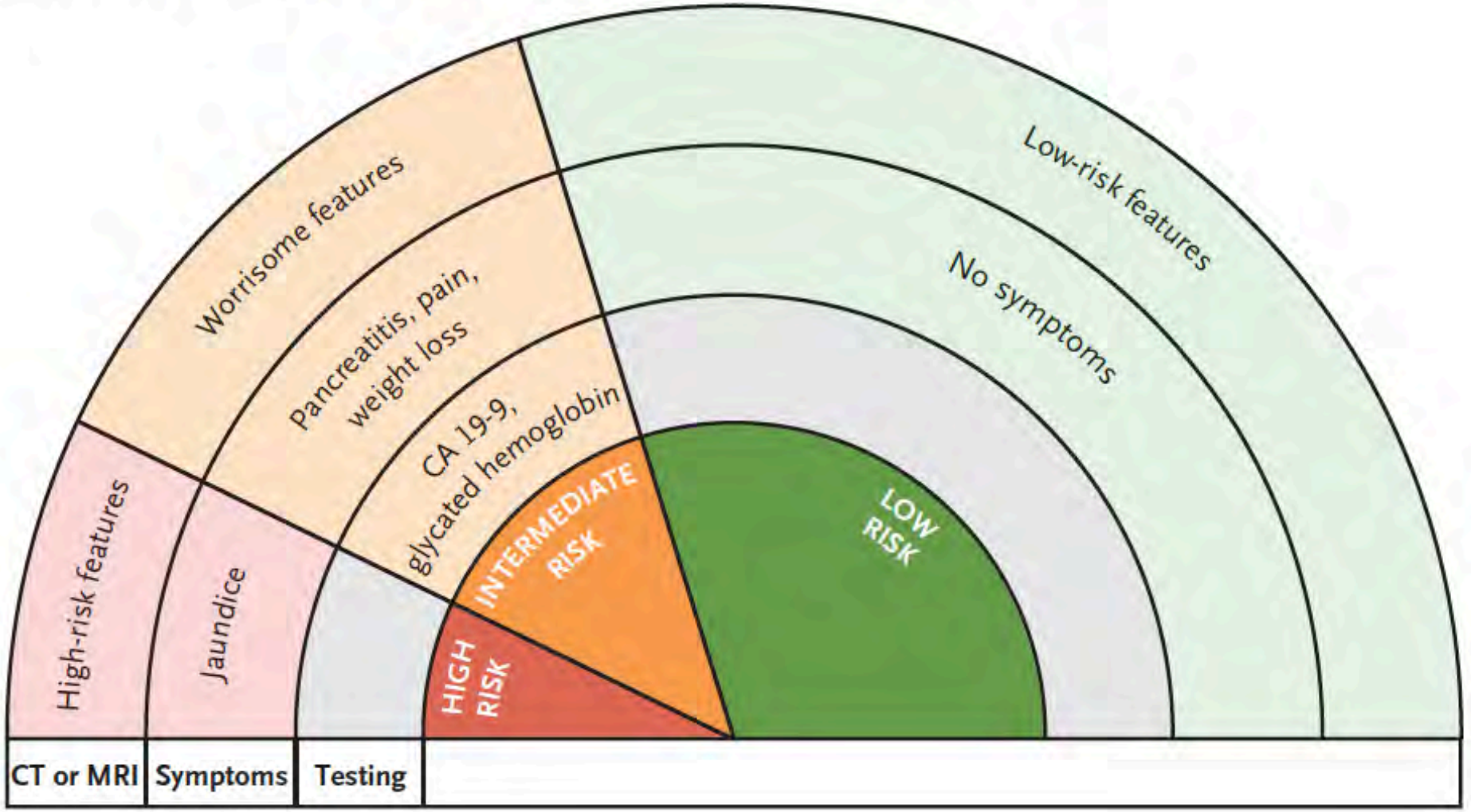
Stuppner S. *Radiopaedia.org* 2015

Cyst Type	Patient Characteristics and Clinical Presentation		Imaging Findings		Malignant Potential
Pseudocyst	Associated with antecedent acute or chronic pancreatitis		Unilocular or multilocular May be connected to MPD		0%
SCA	Predominantly in women (60% of cases) Occurs in 5th–7th decades of life Mostly asymptomatic		Microcystic or oligocystic Central scar No communication with pancreatic duct		0%
IPMN	Equal sex distribution Occurs in 5th–7th decades of life Mostly asymptomatic May cause pancreatitis	 Branch-duct IPMN	Communication with pancreatic duct Multiplicity		1–38%
		 Main-duct IPMN	MPD dilatation Fish-mouth papilla		33–85%
MCN	Almost exclusively in women (90% of cases) Occurs in 4th–6th decades of life Mostly asymptomatic		Mostly pancreatic tail Unilocular or oligolocular Thickened wall Eggshell calcifications in 25%		10–34%
SPT	Almost exclusively in women (90% of cases) Occurs in 2nd or 3rd decade of life Mostly asymptomatic		Heterogeneous Eggshell calcifications		10–15%
CNET	Variable age and sex Mostly asymptomatic 10% Are functional		Enhancing, thickened wall		5–10%

Gonda TA et al *NEJM.* 2024

ASSESSING FOR MALIGNANCY RISK

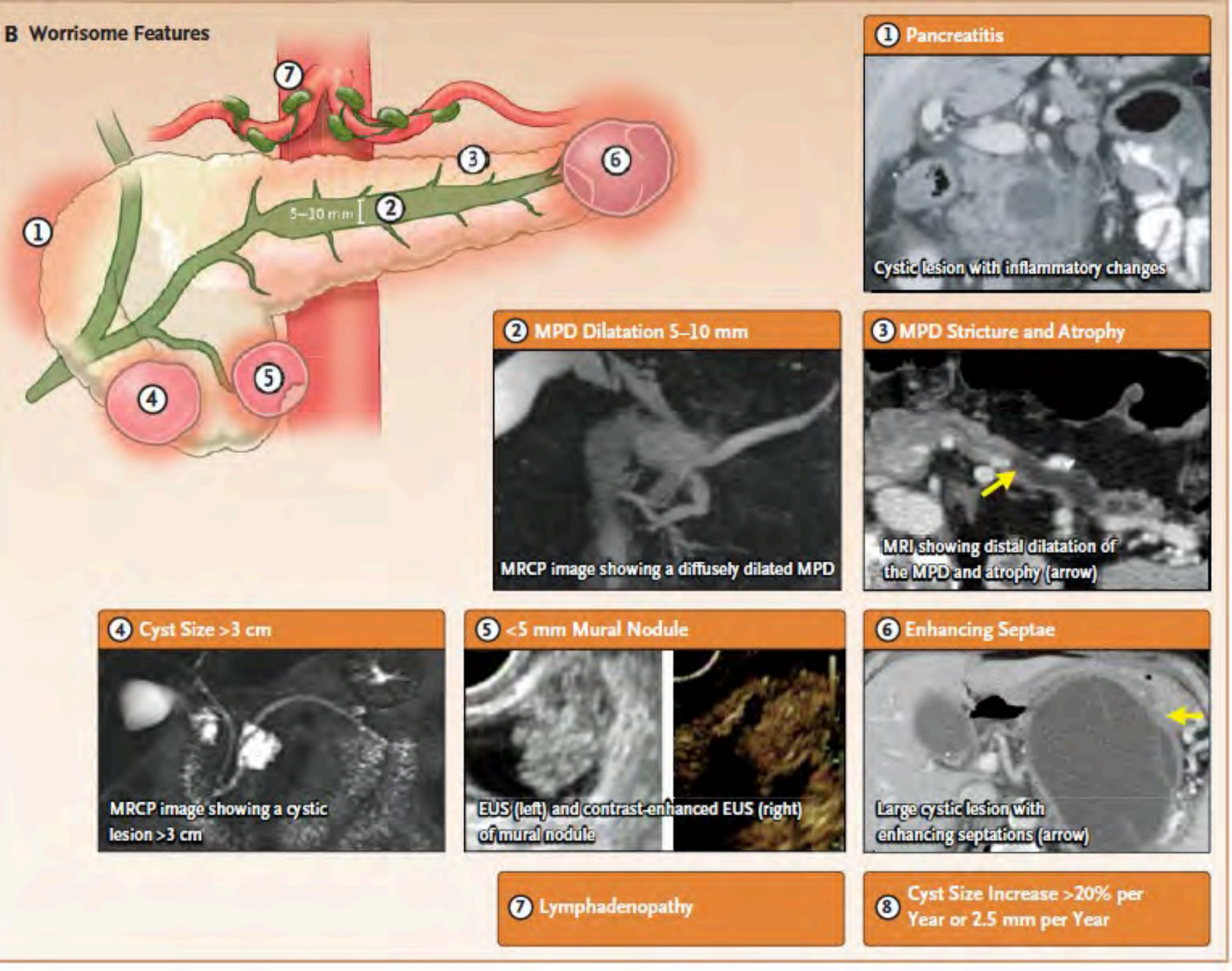
A Approach to the Assessment of Cancer Risk in Patients with Pancreatic Cysts



Gonda TA et al. 2024

HIGH RISK STIGMATA ON IMAGING

Gonda TA et al. 2024



Worrisome features on imaging

Gonda TA et al. NEJM 2024

SYMPTOMS

High risk

- Jaundice

Intermediate risk

- Pancreatitis
- Abdominal pain
- Weight loss

LABS

- Intermediate risks
  - High Ca 19-9
  - New diagnosis of DM- high Hb A1c

RISK CATEGORIES

- Inequivocally benign
  - Pseudocyst
  - SCA
  - No need for further malignancy work up
  - Managed based on symptoms
- Low risk
  - Small mucinous cysts
  - BD-IPMNs
- Intermediate/high risk
  - Mucinous cysts (MD-IPMNs, mixed duct IPMNs)
  - SPN
  - Cystic pNETs
  - Cystic degeneration of solid carcinoma

ENDOSCOPIC EVALUATION

- EUS
  - Serves to further risk-stratify intermediate risk patients
  - Confirms low risk diagnosis
  - In high risk, can help to establish pre-op diagnosis of advanced neoplasia
  - Better accuracy than MRI: nodules, ductal connection
  - FNB- targeted if solid component is found
- Demonstration of fish-mouth in MD-IPMNs

FLUID ANALYSIS

- Yield for cytological diagnosis is low
- Amylase
  - Elevated levels indicate communication with PD
  - Found in IPMNs, pseudocysts
- CEA
  - High levels in mucinous cysts, very low levels rules them out
- Glucose
  - Low levels found in mucinous cysts

FLUID ANALYSIS

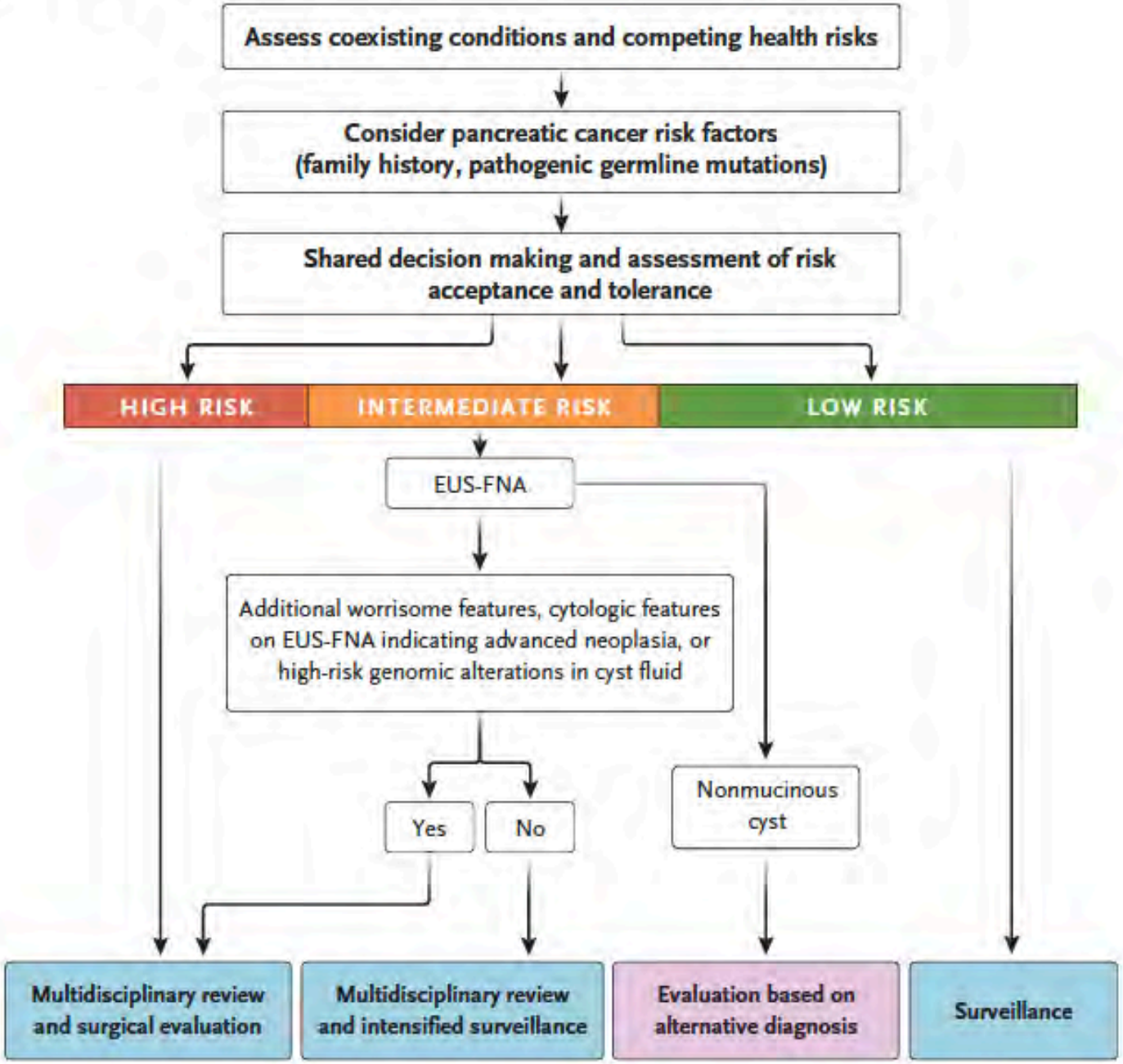
- DNA analysis for mutations especially if other features are inconclusive
  - VHL: 100% specific for SCA, but only found in 25-50%
  - *K-ras*: mucinous cyst
  - GNAs: IPMNs (not MCN)
  - CTNNB1: SPN
  - MEN1: pNET
- Mutation analysis for risk of advanced neoplasia
  - P53, CDKN2A, CTNNB1, SMAD4

Table 1. Cyst-Fluid Characteristics and Genes Altered in Common Types of Pancreatic Cysts.*

Cyst Type	Macroscopic and Cytologic Features	CEA Level	Glucose Level	Amylase Level	Altered Genes	
					Associated with Cyst Type	Associated with Advanced Neoplasia
Pseudocyst	Macrophages and lymphocytes, debris	Variable	High	High	None	None
SCA	Proteinaceous debris and blood, glycogen-rich cuboidal epithelial cells	Very low	High	Low	*VHL*	None
IPMN	Thick mucinous fluid, mucinous epithelial cells, papillary structures†	High	Low	High	*KRAS*, *GNAS*	*TP53*, *CTNNB1*, *CDKN2A*, *SMAD4*, genes involved in mTOR pathway‡
MCN	Thick mucinous fluid, mucinous epithelial cells, ovarian-type stroma†	High	Low	Low	*KRAS*	*TP53*, *CDKN2A*, *CTNNB1*, *SMAD4*, genes involved in mTOR pathway‡
SPT	Hemorrhagic debris; monomorphic, discohesive small cells; hyaline globules and grooved nuclei	Variable	Normal	Low	*CTNNB1*	None
CNET	Uniform cells in loosely cohesive clusters; coarse, granular, chromatin-containing nuclei	Variable	Normal	Low	*MEN1*	None

Gonda TA et al. 2024

B Algorithm for the Management of Presumed Mucinous Cystic Lesions



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Surveillance for mucinous cysts

Cyst Size and Features	Year 1	Years 2–5	After >5 Years of Stability
<1 cm without worrisome features or high-risk stigmata	**12 Months** • MRI • Measurement of CA 19-9 and glycated hemoglobin levels	**Every 2 years** • MRI • Measurement of CA 19-9 and glycated hemoglobin levels	**Every 2 years** • MRI • Measurement of CA 19-9 and glycated hemoglobin levels **Or consider** • Ceasing surveillance
1–2 cm without worrisome features or high-risk stigmata	**6–12 Months** • MRI • Measurement of CA 19-9 and glycated hemoglobin levels	**Every 1–2 years** • MRI • Measurement of CA 19-9 and glycated hemoglobin levels	**Every 2 years** • MRI • Measurement of CA 19-9 and glycated hemoglobin levels **Or consider** • Ceasing surveillance
2–3 cm without worrisome features or high-risk stigmata	**Alternating every 6 months** • MRI or endoscopic ultrasonography • Measurement of CA 19-9 and glycated hemoglobin levels	**Either in 6–12 months** • MRI or endoscopic ultrasonography • Measurement of CA 19-9 and glycated hemoglobin levels	**Every year** • MRI • Measurement of CA 19-9 and glycated hemoglobin levels • Continue surveillance
>3 cm or worrisome features (when surgical resection is not pursued)	**Alternating every 3 months** • MRI or endoscopic ultrasonography • Measurement of CA 19-9 and glycated hemoglobin levels	**Alternating every 3–6 months** • MRI or endoscopic ultrasonography • Measurement of CA 19-9 and glycated hemoglobin levels	**Every 6–12 months** • MRI • Measurement of CA 19-9 and glycated hemoglobin levels • Continue surveillance

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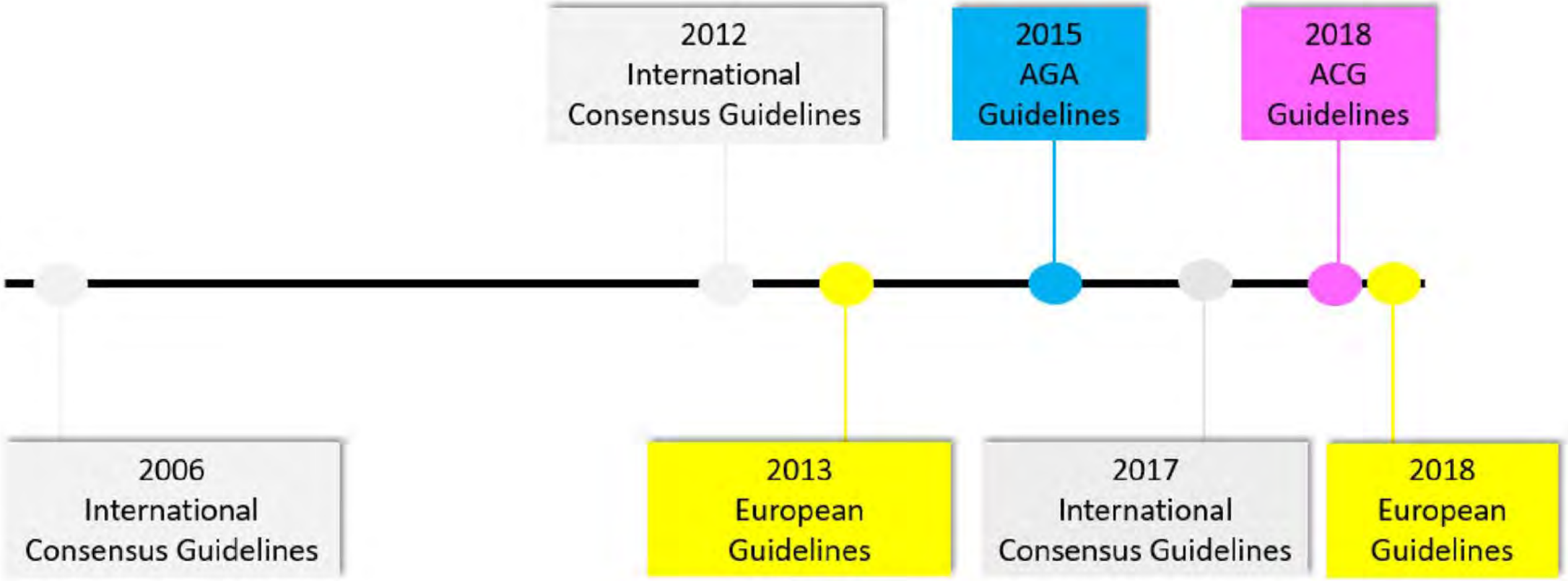
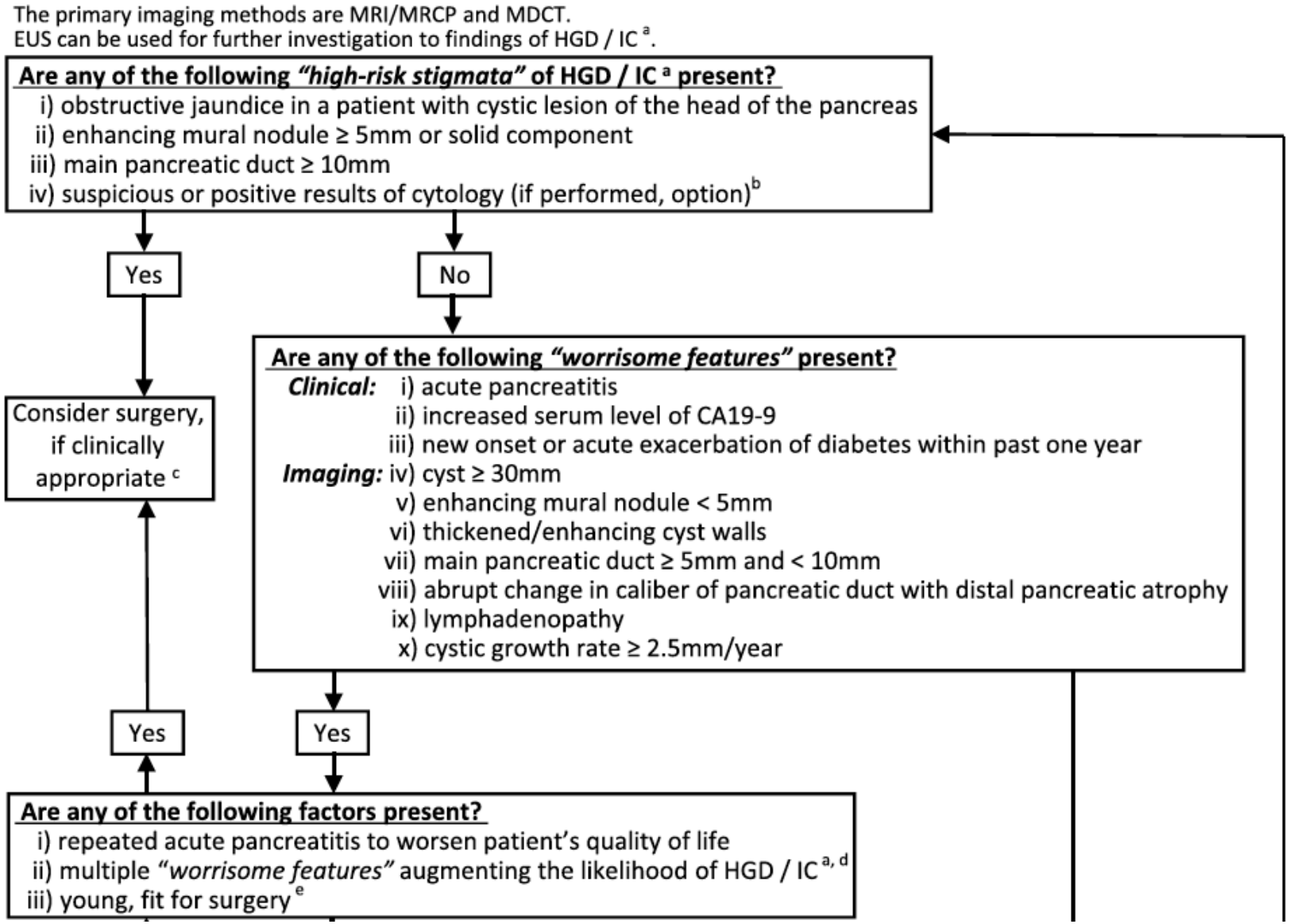
AVAILABLE GUIDELINES

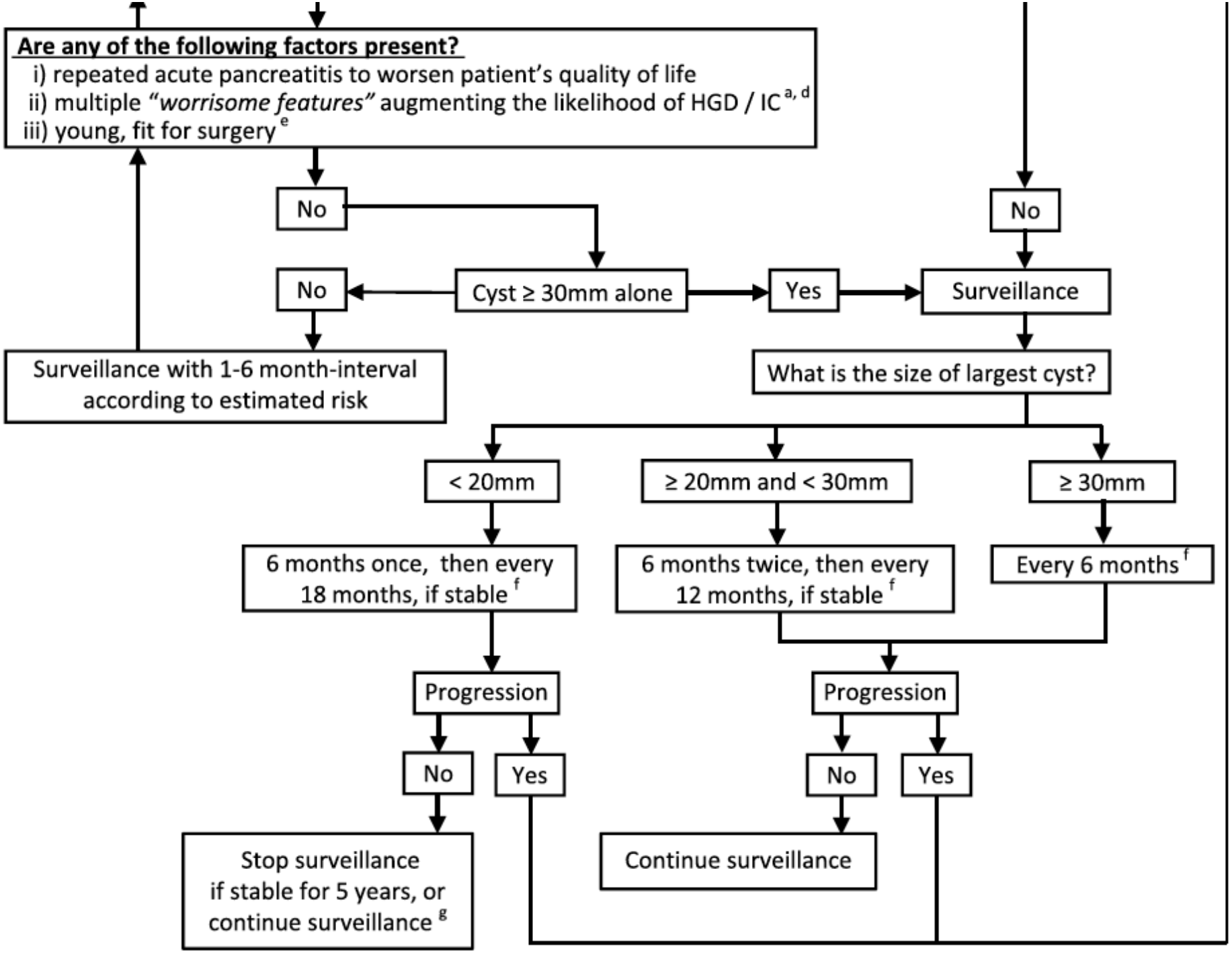


timeline

KYOTO BD-IPMN MANAGEMENT GUIDELINE



Ohtsuka T eta al.
Pancreatology 2024



Ohtsuka T eta al.
Pancreatology 2024

SURVEILLANCE FOR LOW RISK CYSTS (IPMN)

	Surveillance of low-risk pancreatic cystic lesions
AGA 2015	<1 cm: MRI/CT at 1 y then every 2 y × 5 y
IAP 2017 (BD-IPMN only)	<1 cm: MRI/CT at 6 mo then every 2 y 1–2 cm: MRI/CT every 6 mo × 1 y, then every 1 y × 2 y, then every 2 y 2–3 cm: EUS in 3–6 mo, then EUS alternate with MRI every 1 y >3 cm: MRI alternate with EUS every 3–6 mo
ACR 2017 (for patients <65 y)	<1.5 cm: MRI/EUS/CT every 1 y × 5 y then every 2 y × 2 1.5–1.9 cm with MPD communication: MRI/CT/EUS every 1 y × 5 then every 2 y × 2 2.0–2.5 cm with MPD communication: MRI/CT/EUS every 6 mo × 4, then every 1 y × 2, then every 2 y × 3 >2.5 cm: MRI/CT/EUS every 6 mo × 4 then every 1y × 2 then every 2y × 3
ACG 2018	<1 cm: MRI every 2 y × 4 y 1–2 cm: MRI every 1 y × 3 y, then MRI every 2 y × 4 y 2–3 cm: MRI or EUS every 6–12 mo × 3 y, then MRI every 1 y × 4 y >3 cm: MRI alternate with EUS every 6 mo × 3 y, then MRI alternate with EUS every 1y × 4y
European 2018	MRI ± EUS every 6 mo × 1 y, than every 1 y until nonsurgical candidate

SURVEILLANCE CESSATION

	Surveillance cessation
AGA 2015	Stop if no significant change in the characteristics of the cyst after 5 y of surveillance or if the patient is no longer a surgical candidate
IAP 2017	Continue indefinitely as long as fit for surgery
ACR 2017 (for patients <65 y)	Stop if cyst <1.5 cm after minimum 10 y
ACG 2018	Surveillance should be discontinued if no longer a surgical candidate. It is reasonable to assess the utility of ongoing surveillance in those aged >75 y. An individualized approach for those aged 76–85 y should be considered, including an informed discussion about surgery.
European 2018	Patients affected by IPMN without indication for surgery should be observed until they are no longer fit for surgery

SUMMARY

- Pancreatic cysts are common and are being discovered at an increasing rate on cross-sectional imaging, but only a minority progress to cancer.
- The most important goal is to identify the small percentage of cystic lesions associated with a substantial risk of cancer, and this should be done through a multidisciplinary evaluation based on an algorithmic approach.
- In many cases, imaging, symptom assessment, and laboratory tests can help distinguish benign cysts from those associated with a low, intermediate, or high risk of malignant transformation.
- Endoscopic ultrasonography should be considered for equivocal findings or intermediate-risk cysts.
- Endoscopic ultrasonography and fluid aspiration for cytologic and molecular analysis may help in risk stratification for patients with intermediate-risk cysts.
- Surgical evaluation is warranted for high-risk cysts and for intermediate-risk cysts with multiple risk features, whereas surveillance is used for low-risk cysts.

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