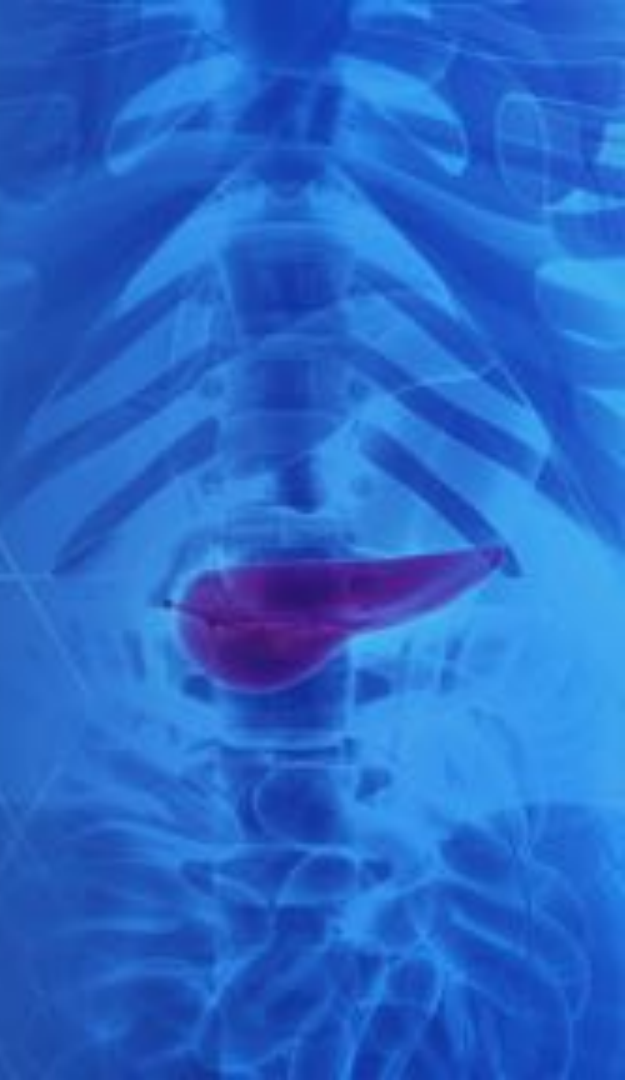
2018 CAPER Collaborative Alliance for Pancreatic Education and Research

PANCREAS ACADEMY



Rehoboth McKinley Christian Health Care Services

CAPER Collaborative Alliance for Pancreatic Education and Research

Jointly provided by the New Mexico Medical Society (NMMS) through the joint providership of Rehoboth McKinley Christian Health Care Services (RMCHCS) and the Collaborative Alliance for Pancreatic Education and Research.

2018 CAPER
PANCREAS ACADEMY

Overview of Pancreatic Cysts: Diagnosis and Management

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Disclosures

- No Relevant Disclosures

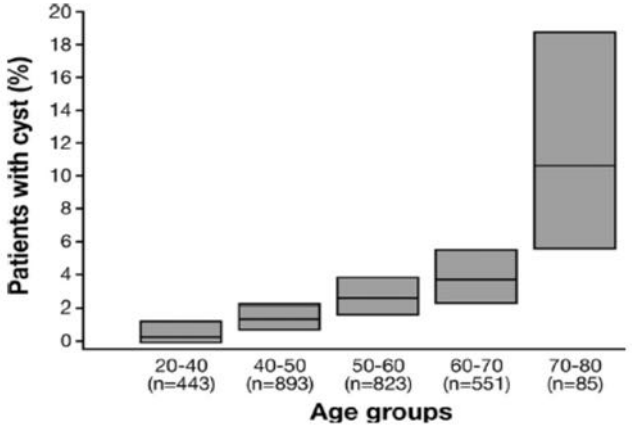
Pancreatic Cysts

- Background
- Diagnosis & Management

Frequency of Incidental Cysts

Study	Test	N	Mean Age	Male (%)	Cyst (%)	Median Size
Laffan et. al	MDCT	2832	58	51%	**2.6%**	8.9 mm
de Jong et. al	MRI	2803	51	65%	**2.4%**	8.0 mm

≈ 2 - 3 million people in the U.S



Laffan, TA, et. al. AJR Am J Roentgenol 2008:802-7
de Jong, K. et. al. Clin Gastroenterol Hepatol 2010:806-11

Why do we care?

- 3 recognized precursor lesions to pancreatic adenocarcinoma
  - Mucinous Cystic Neoplasm (MCN)
  - Intraductal Papillary Mucinous Neoplasm (IPMN)
  - Pancreatic Intraepithelial Neoplasms (PanIN)
- ~ 15% of pancreatic adenocarcinomas arise from pancreatic cysts.

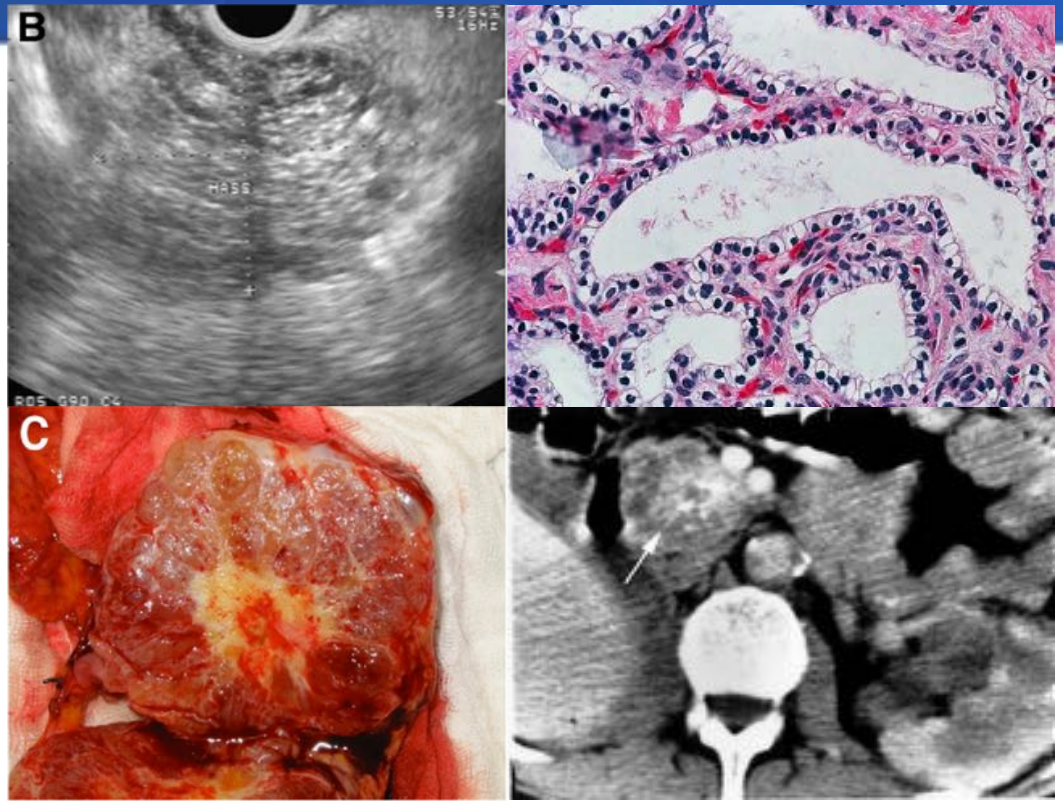
Hruban, RH, et. al. Gastroenterol Clin North Am 2007:831-49
Adsay, NV. Mod Pathol 2007: S71-93

Most Common Cysts

CYST TYPE	AGE	GENDER	LOCATION
Serous Cystic Neoplasm	70's	F>M	Body/Tail > Head
Mucinous Cystic Neoplasm	50's	F>>M (95%)	Body/Tail >>Head
Intraductal Papillary Mucinous Neoplasm	70's	F=M	Head > Body/Tail

Brugge, W. NEJM 2004:1218-26

Serous Cystic Neoplasm



Khalid A. Am J Gastroenterol 2007: 2339-49
Al-Haddad, M, et. al. Clin Gastro Hepatol 2011:635-48

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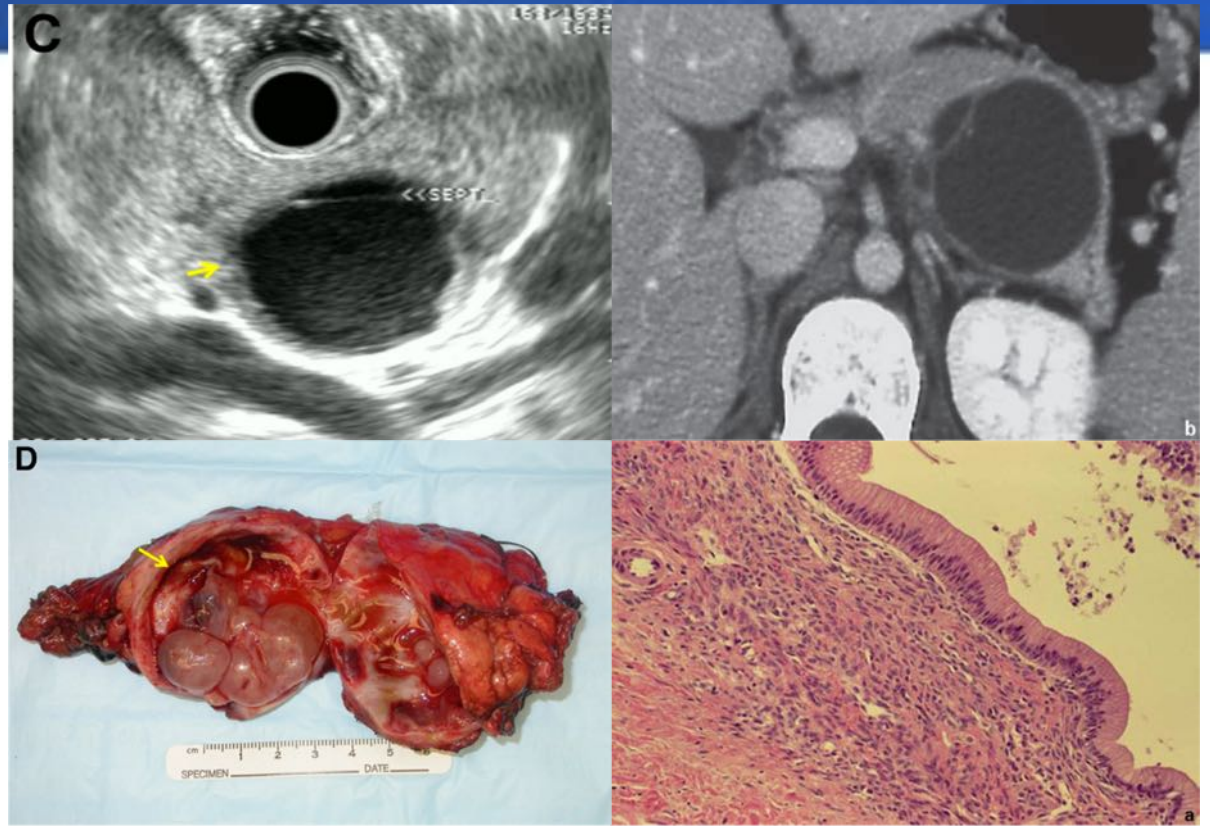
Brugge, W. NEJM 2004:1218-26

Mucinous Cystic Neoplasm



Tanaka M. Pancreatology 2006: 17 – 32
Al-Haddad, M, et. al. Clin Gastro Hepatol 2011:635-

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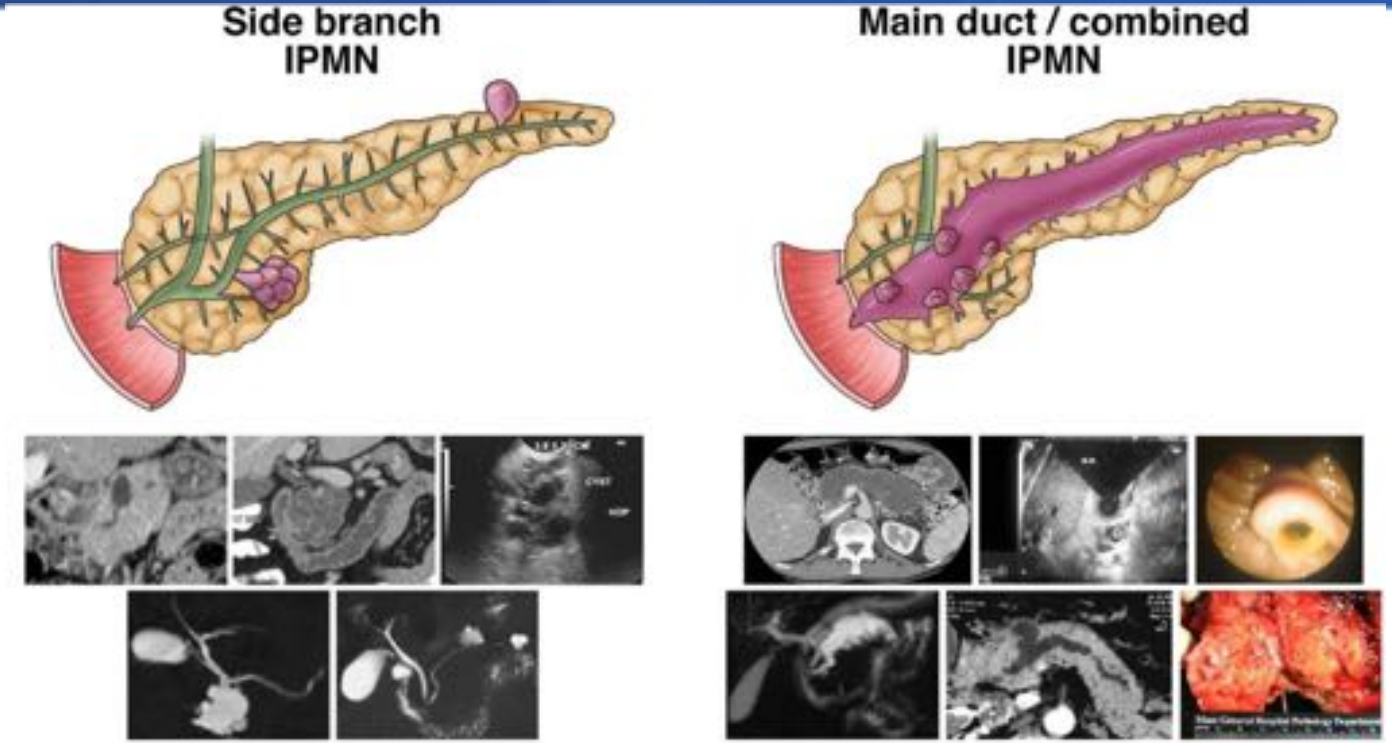
Intraductal Papillary Mucinous Neoplasm



Fernandez-del Castillo, C, et. al. Gastroenterology 2010:708-13

Frequency of Malignancy

Cyst Type	% Malignant
Serous Cystic Neoplasm	0%
Mucinous Cystic Neoplasm	15%
Intraductal Papillary Mucinous Neoplasm	
Main Duct Disease	60%
Branch Duct Disease	24%

Tanaka M. Pancreatology 2012: 183 - 97

Pancreatic Cysts

- Background
- Diagnosis & Management

Pancreatology

Review

Pancreatology 2006;6:17–32
DOI: 10.1159/000090023

Published online: November 29, 2005

International Consensus Guidelines for Management of Intraductal Papillary Mucinous Neoplasms and Mucinous Cystic Neoplasms of the Pancreas

Masao Tanaka[a] Suresh Chari[b] Volkan Adsay[c]
Carlos Fernandez-del Castillo[d] Massimo Falconi[e] Michio Shimizu[f]
Koji Yamaguchi[a] Kenji Yamao[g] Seiki Matsuno[h]

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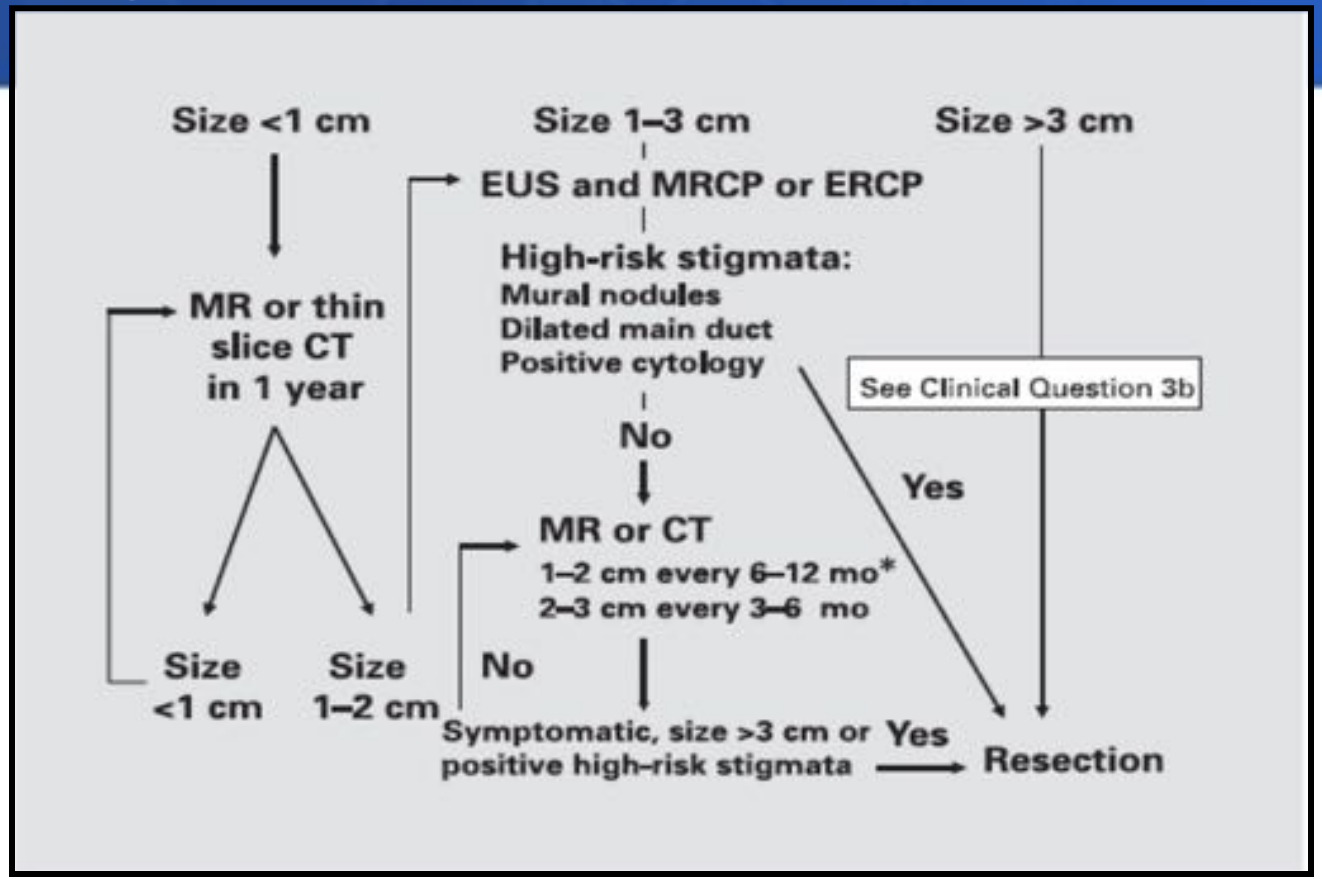
Sendai Criteria (2006)

Cyst Type	Treatment
Serous Cystic neoplasm	Reassure with no follow-up
Mucinous Cystic Neoplasm	Resect
Intraductal Papillary Mucinous Neoplasm	
Main Duct	Resect
Branch Duct	Observe/Resect

Tanaka M. Pancreatology 2006:17-32

Algorithm for Branch Duct IPMNs



Tanaka M. Pancreatology 2006:17-32

Performance of Sendai Criteria

Author	# Resected Cysts	Sensitivity for Malignancy	Specificity for Malignancy	PPV for Malignancy	NPV for Malignancy
Palaez-Luna (2007)	77 (9 cancers)	100% (9/9)	23% (16/68)	14% (9/61)	100% (16/16)
Rodriguez (2007)	145 (32 cancers)	100% (32/32)	NR	NR	NR
Tang (2008)	31 (5 cancers)	100% (5/5)	31% (8/26)	22% (5/23)	100% (8/8)

Palaez-Luna, M. et al. Clin Gastroenterol Hepatol 2007;1759-64
Rodriguez, JR, et. al. Gastroenterology 2007;72-9
Tang, RS, et. al. Clin Gastroenterol Hepatol 2008;815-9

Pancreatology 12 (2012) 183–197

Contents lists available at SciVerse ScienceDirect

Pancreatology

journal homepage: www.elsevier.com/locate/pan

Review article

International consensus guidelines 2012 for the management of IPMN and MCN of the pancreas

Masao Tanaka [a,*], Carlos Fernández-del Castillo [b], Volkan Adsay [c], Suresh Chari [d], Massimo Falconi [e], Jin-Young Jang [f], Wataru Kimura [g], Philippe Levy [h], Martha Bishop Pitman [i], C. Max Schmidt [j], Michio Shimizu [k], Christopher L. Wolfgang [l], Koji Yamaguchi [m], Kenji Yamao [n]

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[i] Department of Pathology, Massachusetts General Hospital, Harvard Medical School, Boston, MA, USA
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[k] Department of Pathology, Saitama Medical University, International Medical Center, Saitama, Japan
[l] Cameron Division of Surgical Oncology and The Sol Goldman Pancreatic Cancer Research Center, Department of Surgery, Johns Hopkins University, Baltimore, MD, USA
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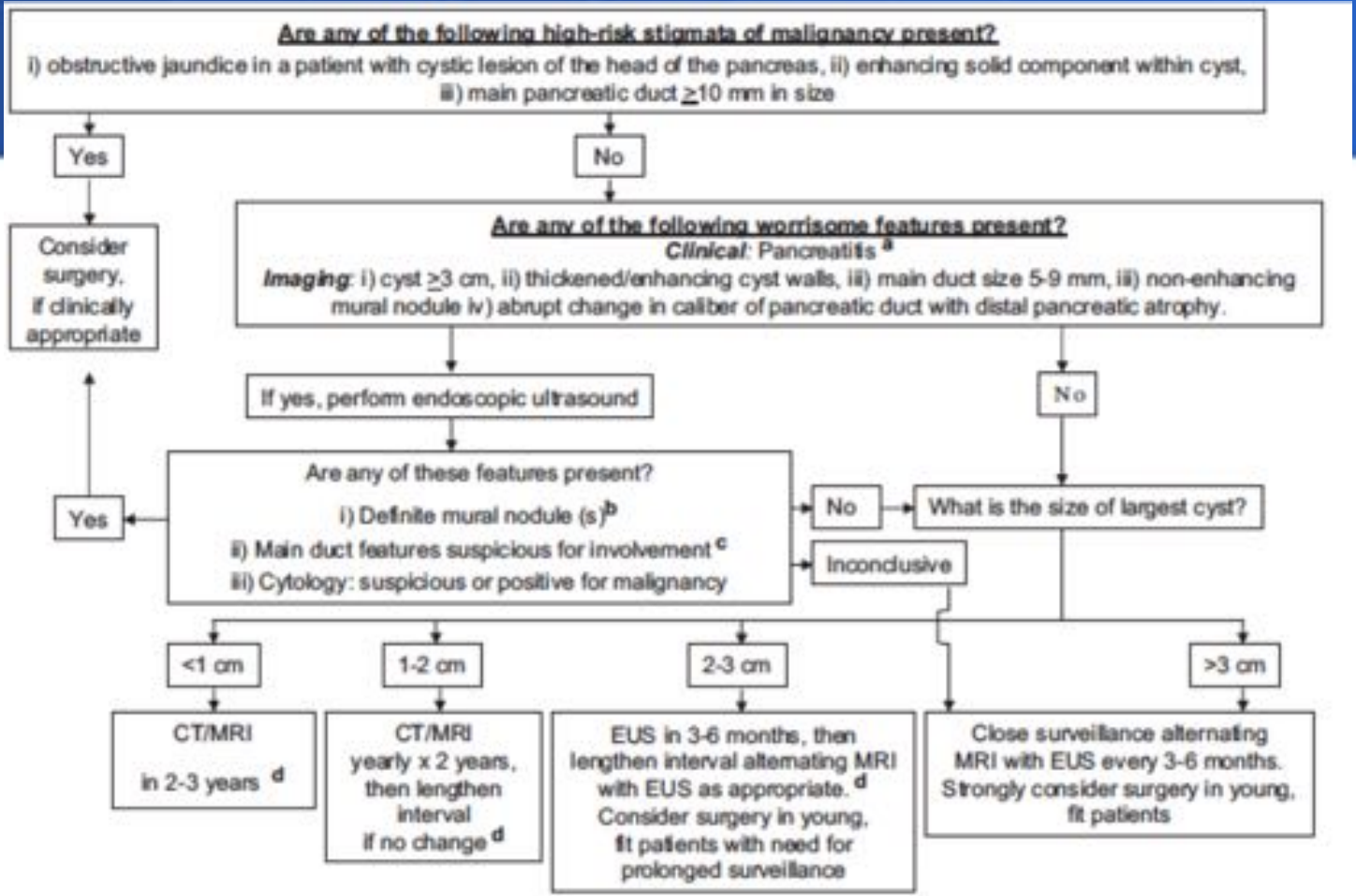
[n] Aichi Cancer Center Hospital, Aichi, Japan

Resection Criteria for Branch Duct IPMNs

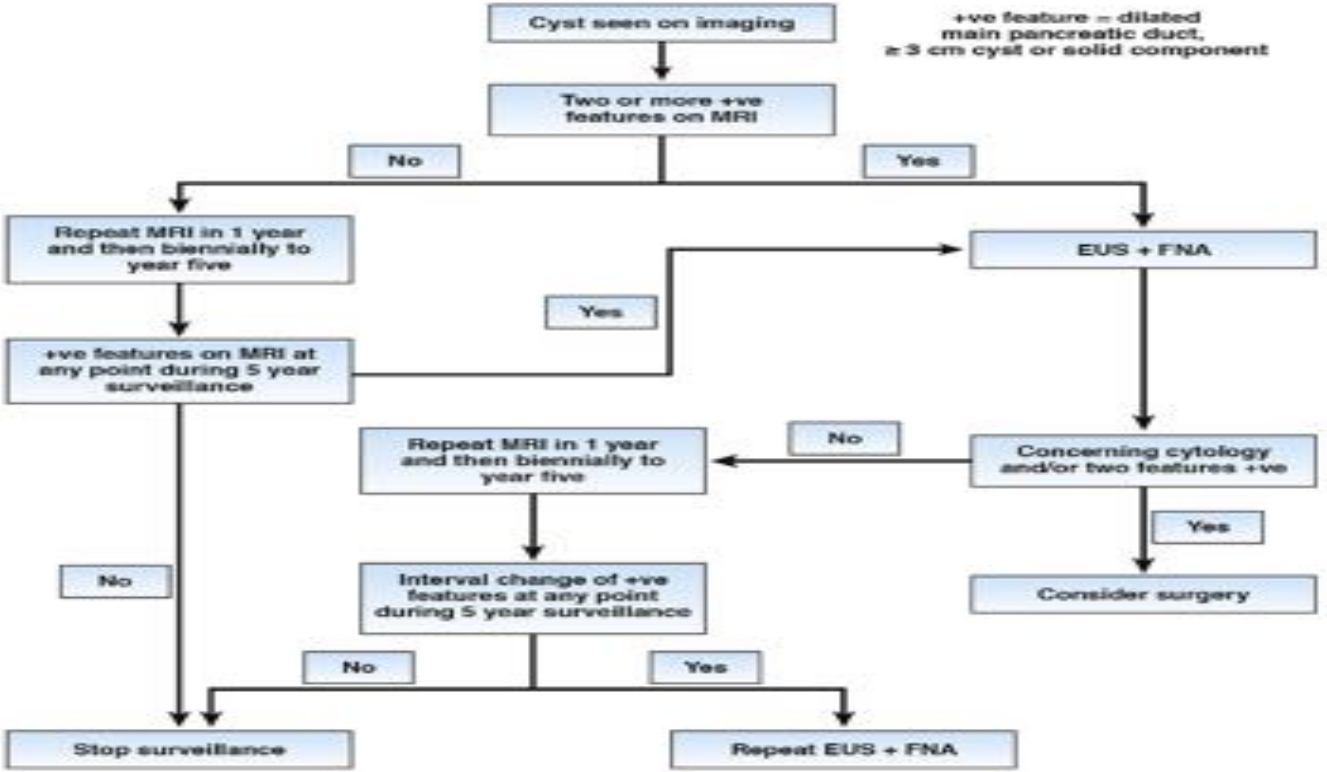
Sendai Criteria (2006)	Fukuoka Criteria (2012)
Size > 3 cm	Size cutoff abandoned
Presence of mural nodule	Presence of ENHANCED mural nodule
Dilated main duct > 6 mm	Dilated main duct > 10 mm
Symptomatic	Obstructive Jaundice
Positive Cytology	Unchanged

Tanaka M. Pancreatology 2012: 183 - 97



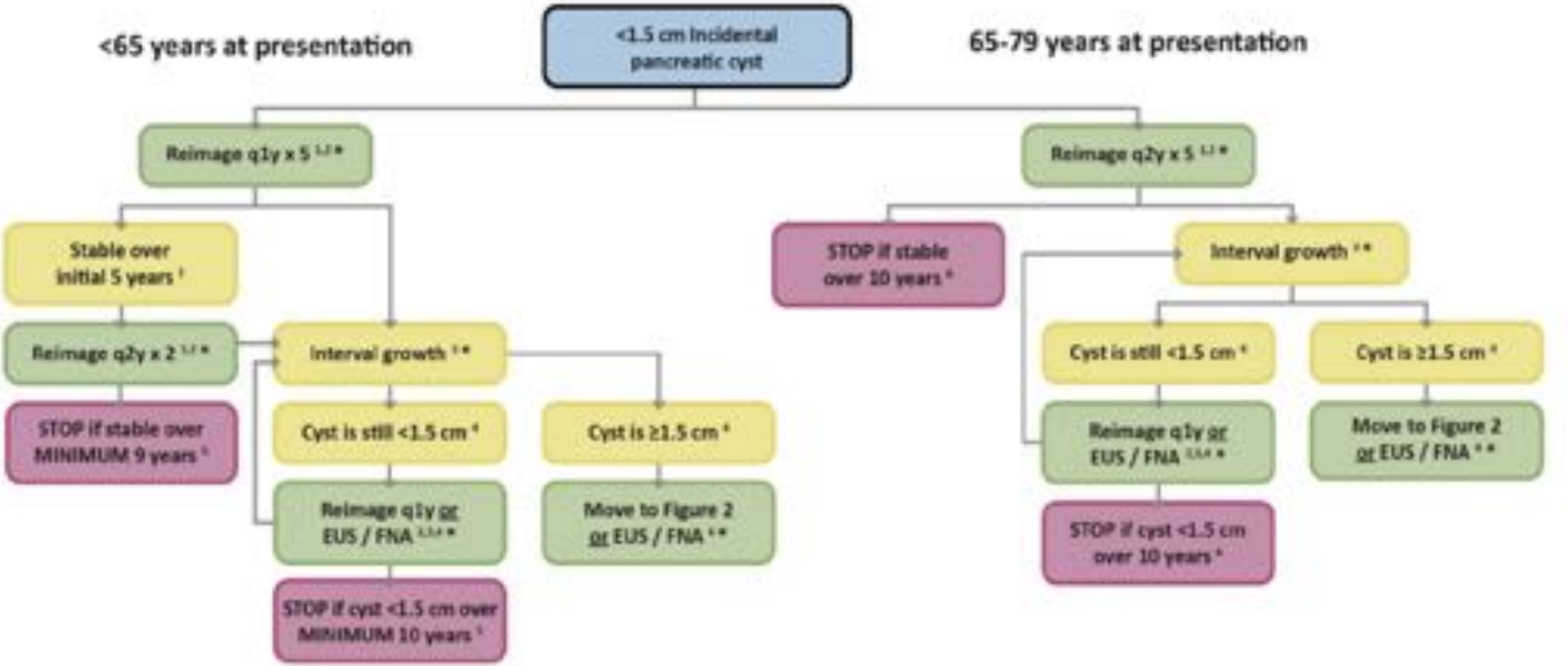
Tanaka M. Pancreatology 2012: 183 - 97

AGA Guidelines



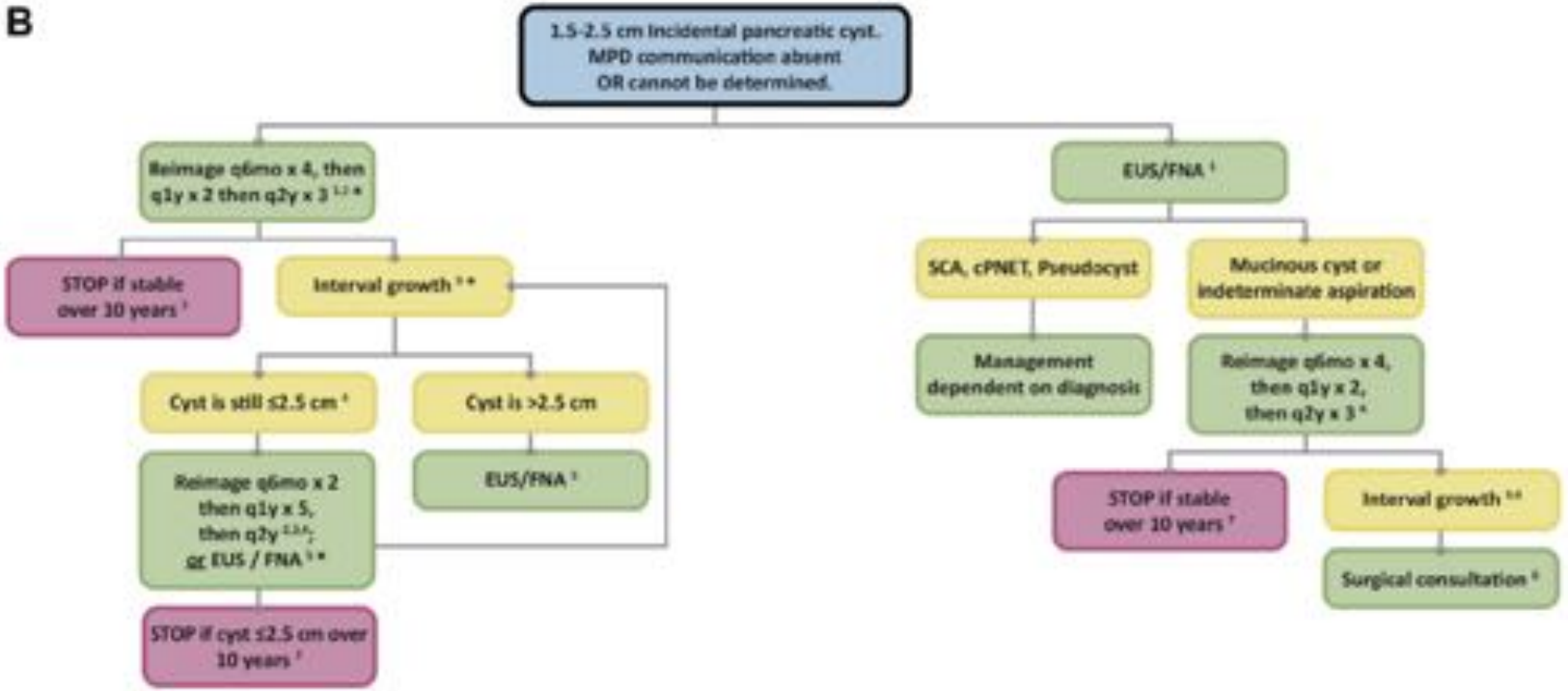
Gastroenterology 2015;823

American College of Radiology



Megibow A et al . J Am Coll Radiol 2017: 911-923

American College of Radiology



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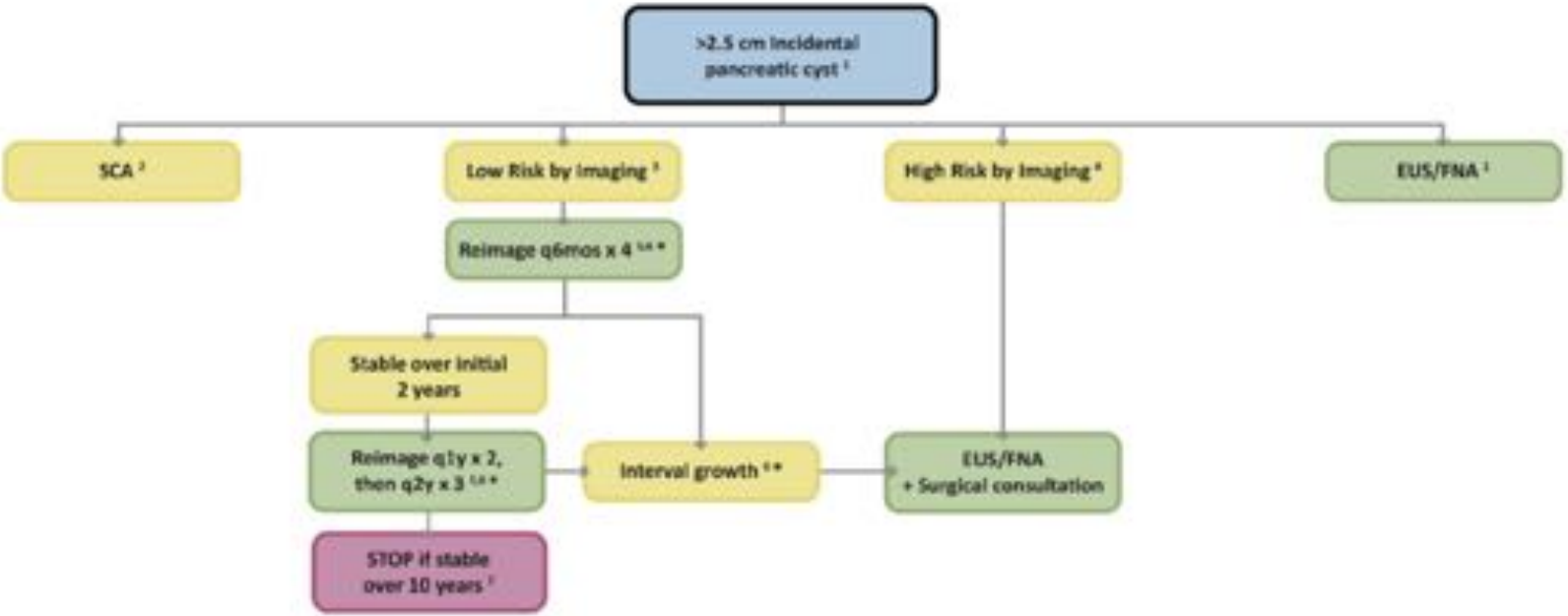

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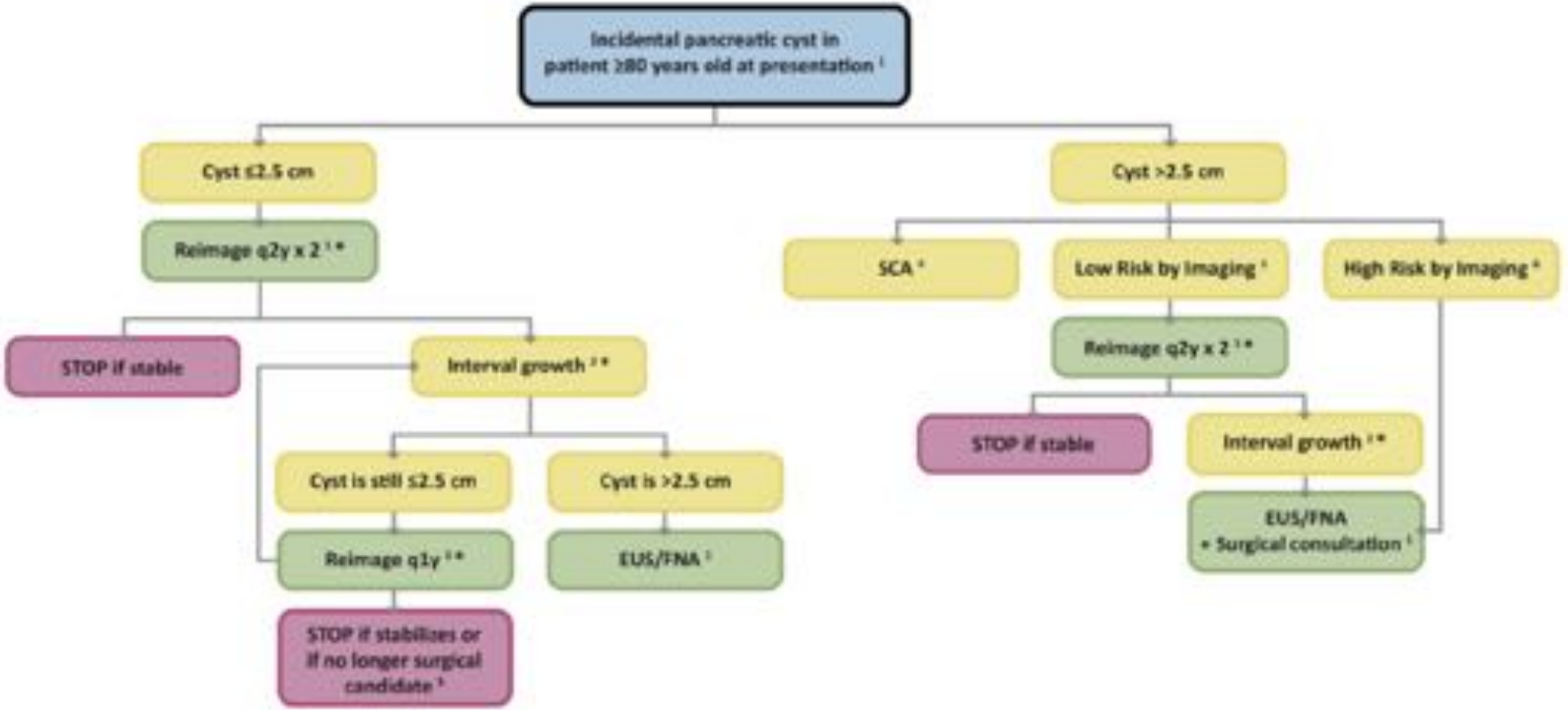
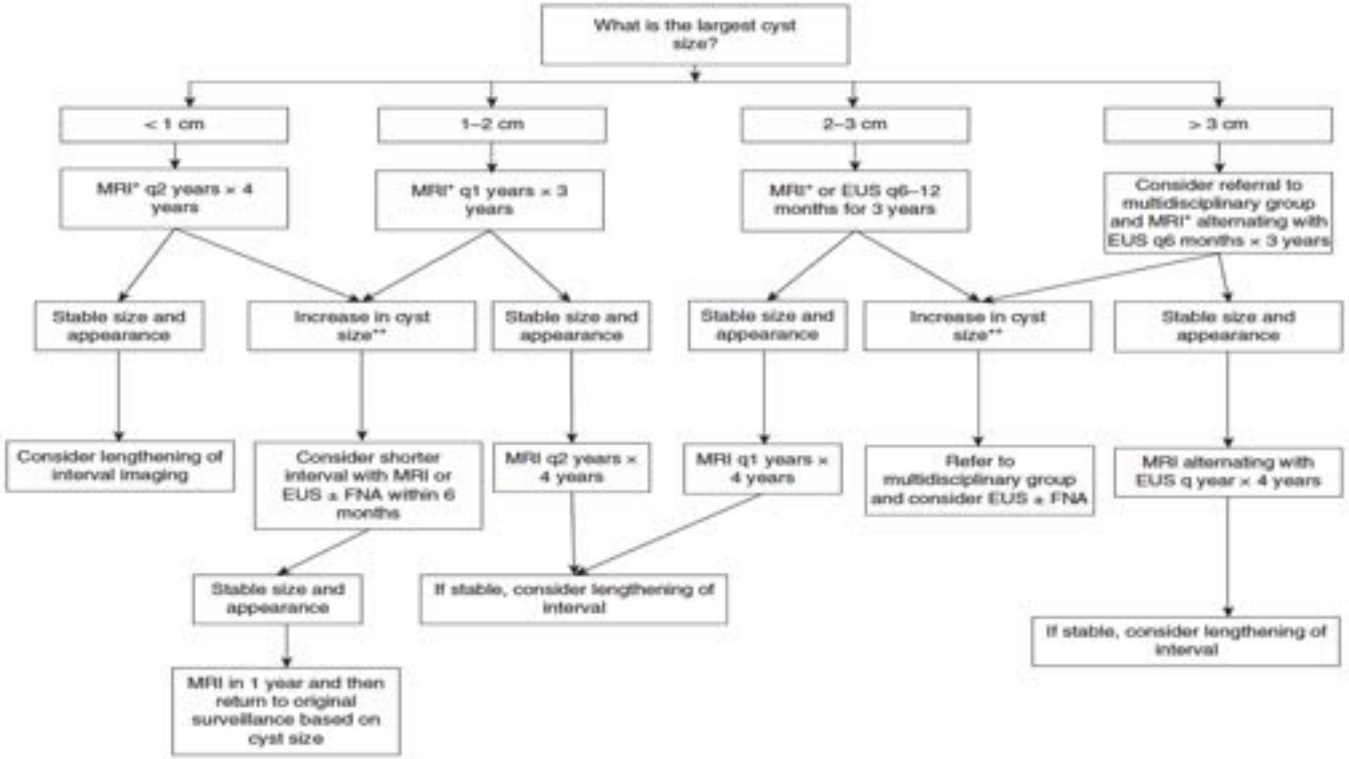


Megibow A et al . J Am Coll Radiol 2017: 911-923

American College of Gastroenterology

Elta GH et al. Am J Gastroenterol 2018: epub

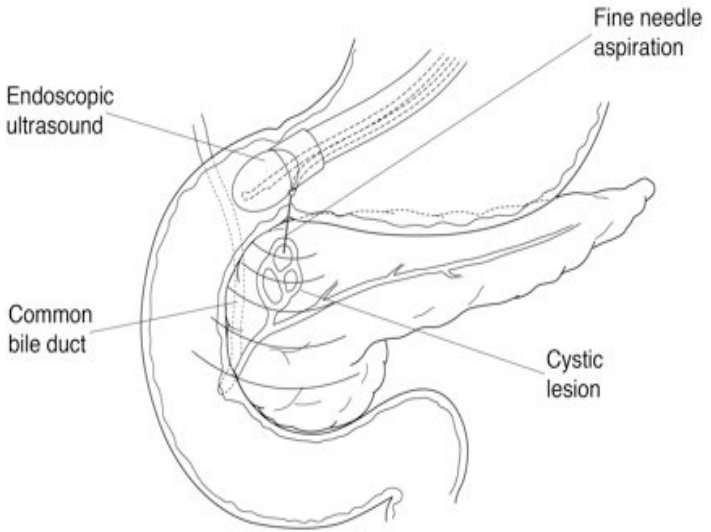
American College of Gastroenterology



Elta GH et al. Am J Gastroenterol 2018: epub

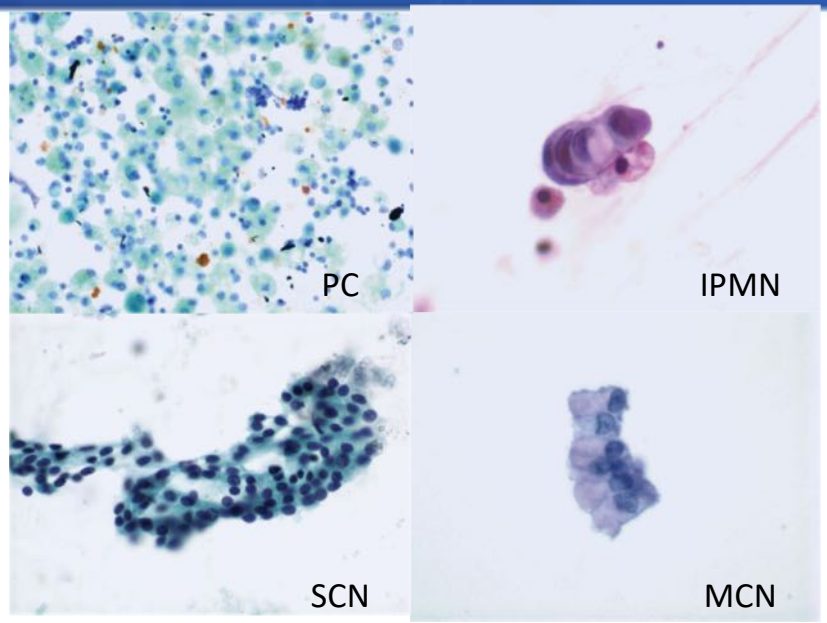
Virtues of the Cyst Fluid Space

- **Protected space:**
  - Relatively high concentration of secreted proteins, genetic material (DNA), and metabolites
- **Relatively accessible (EUS)**



Cytology

- Limited diagnostic yield (20 - 30%)
- Higher with mural nodules (60 – 75%)



Fernandez-del Castillo C Arch Surg 2003:427-34
Vignesh S. J Clin Gastroenterol 2008:493-506
Pitman, MB, et. al. Cancer Cytopathol 2010:1-13

Cyst Fluid Analysis

- Rationale: Mucinous cysts can be identified from differential secretion of glycoproteins.
- Multi-center study: 112 patients w/ histology

Tumor marker	Sensitivity	Specificity	Accuracy	ROC	*P* value[a]	Cut off
CEA	.73	.84	.79	.7930	<.001	192
CA125	.83	.37	.60	.5910	.183	9
CA15-3	.19	.94	.57	.5011	.816	121
CA19-9	.68	.62	.66	.6654	.004	2900
CA72-4	.80	.61	.72	.7423	.001	7

Brugge WR. Gastroenterology 2004:1330-36

Novel Cyst Biomarkers

Biomarker	Summary Highlights
DNA: *KRAS, GNAS*	- *KRAS:* Differentiate mucinous cysts with a sensitivity of 45% and specificity of 96% - IPMNS: *GNAS* 66%, *KRAS* + *GNAS* 96%
Protein Targets	- High-risk IPMN showed elevated cyst fluid concentrations of MUC2 and MUC4. - MUC5 + CA 19-9 could differentiate mucinous cysts with a sensitivity of 87% and specificity of 88% - AREG 83% sensitivity and 73% specificity for IPMN cancers
Cytokine Profiling	- IL-1Beta could differentiate high Risk IPMN vs. Low Risk IPMN (ROC = 0.92)
mi-RNA	↑ miR-21, miR-221 expressed within malignant cyst fluid.
Other	- VEGF-A 100% sensitivity and 97% specificity for Serous Cystic Neoplasms - mAb Das-1 highly sensitive (89%) and specific (100%) for detecting high risk/malignant IPMNs. - Glucose 94% Sensitivity, 65% specificity for MCNs & IPMNs

PancreaSeq Panel

- KRAS, GNAS, VHL, CTNNB1, TP53, PIK3CA, PTEN mutations
- N=102 samples
- KRAS and/or GNAS
  - 89% sensitivity, 100% specificity for IPMNs & MCNs
- KRAS and/or GNAS and TP53, PIK3CA, PTEN
  - 79% sensitivity, 96% specificity for Advanced Neoplasms

A. Singhi et al. Gut 2017: epub

Conclusions: Consensus or Chaos?

Pancreatic cysts are an *increasingly common* incidentaloma.

Multiple guidelines

Active Surveillance over Resection

Novel Cyst-based Diagnostics