Asymptomatic Pancreatic Cysts What does the evidence tell us?

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Aims

- Clinical significance of pancreatic cysts
- Overview of pancreatic cyst classification
- Highlights of the AGA Technical Review
- Discuss elements of the new AGA Guidelines
  - Compare to international consensus guidelines (Sendai 2012)

Clinical Significance

- Incidence 3-15%
- Risk of malignancy of pancreatic cysts is low
  - 0.01 – 0.25%
- Surgical morbidity and mortality
- Cost of surveillance: $9.3 billion/year (US)

Cyst classification

- Neoplastic cysts
  - Mucinous cystic neoplasms (MCN)
  - Intraductal papillary mucinous neoplasm (IPMN)
    - Main duct
    - Branch duct
    - Mixed
  - Serous cystic neoplasm (SCN)
  - Solid pseudopapillary neoplasm
  - Cystic neuroendocrine tumors

AGA Technical Review – 2015

Gastroenterology 2015;148:824–848

American Gastroenterological Association Technical Review on the Diagnosis and Management of Asymptomatic Neoplastic Pancreatic Cysts

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Methods

- Evidence-based review of >1500 papers
- GRADE (Grading of Recommendations Assessment, Development and Evaluation) framework

Table 1. PICO Questions

	PICO question				
Question	Population(s)	Intervention(s)	Comparator	Outcome(s)	Method
Initial imaging evaluation of pancreatic cysts					
1	Adults with findings of a pancreatic cyst on cross-sectional imaging	Additional MRI imaging	No further investigation	Benefits: Detection of early pancreatic cancer or precancerous cyst Harms: Unnecessary surgery/invasive procedures	RCT, observational studies
2	Adults with concerning findings of a pancreatic cyst on MRI	Additional EUS-FNA	No further investigation	Benefits: Detection of early pancreatic cancer or precancerous cyst Harms: Unnecessary surgery/invasive procedures	RCT, observational studies

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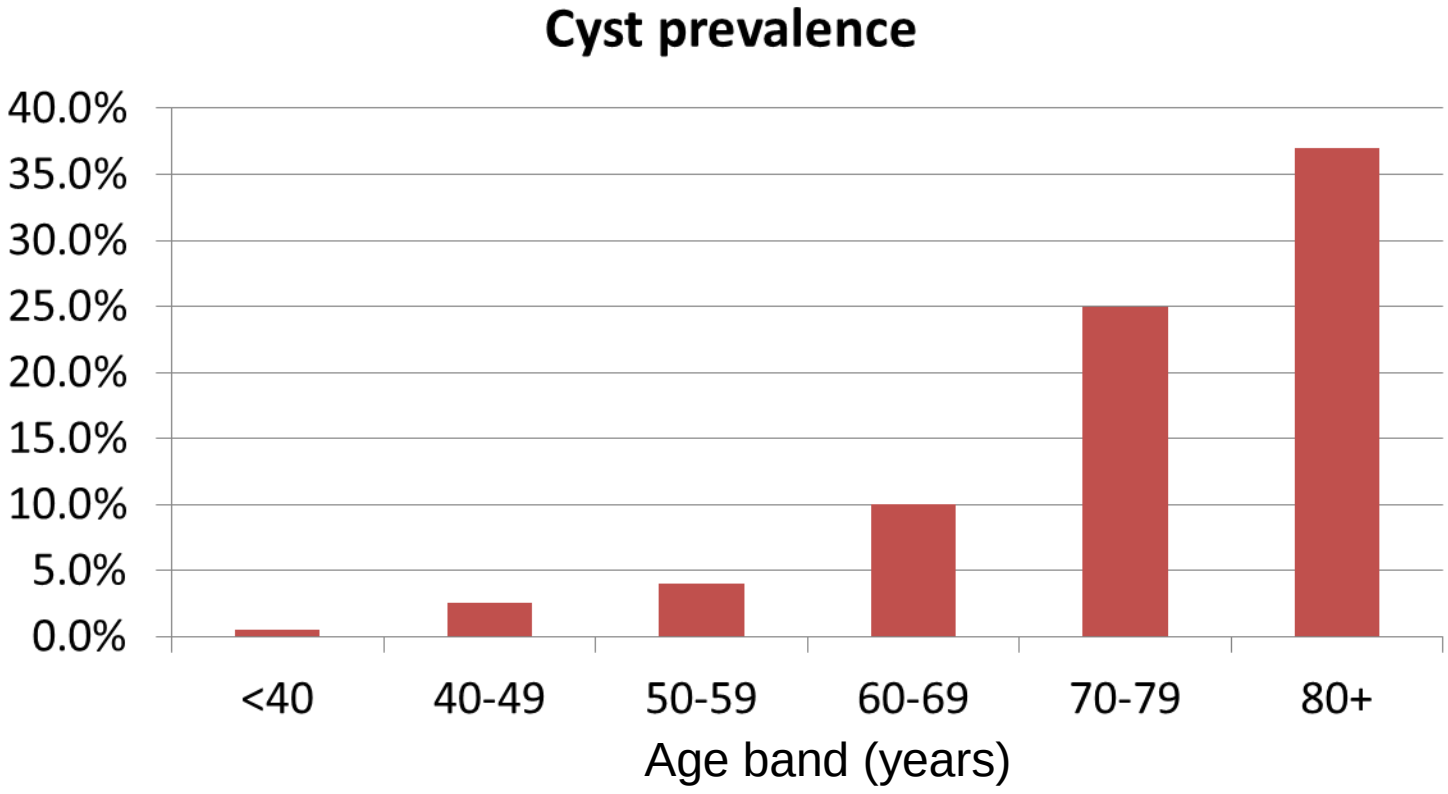
Overall prevalence

- Overall prevalence = 15% (95% CI: 7-24%)



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Imaging Features

- Size of cyst ≥ 3 cm
  - OR 2.97 [1.82-4.85] (6 studies, 644 patients)
- Solid component associate with cyst
  - OR 7.73 [3.38-17.67] (7 studies, 816 patients)
- Dilated pancreatic duct
  - OR 2.38, [0.71-8.00] (4 studies, 609 patients)
- Interval growth
  - OR 1.65 [0.52-5.23] (5 studies, 572 patients)
- Insufficient data to evaluate benefits of cyst fluid analysis, cytology, or molecular testing

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Rate of malignancy

- All cysts – 0.01% risk of malignancy at the time of diagnosis
- Cysts >2 cm – 0.21% risk of malignancy at the time of diagnosis
- Assuming all pancreatic cancer arises from cysts
  - Risk of malignancy at the time of imaging is 0.25%

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Rate of malignancy

- Rate of adenocarcinoma in surgically resected cysts
  - 27 studies, 2796 patients
  - Overall invasive malignancy rate = 15% (95% CI: 12-18%)
- Rate of malignancy in surgically resected IPMNs:
  - 111 studies, 10,812 patients
  - Overall invasive malignancy rate = 25% (95% CI: 23-27%)
- Rate of malignancy in surgically resected MCNs:
  - 12 studies, 603 patients
  - Overall invasive malignancy rate = 15% (95% CI: 9-22%)

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Rate of malignancy is low, even in patients selected for surgery

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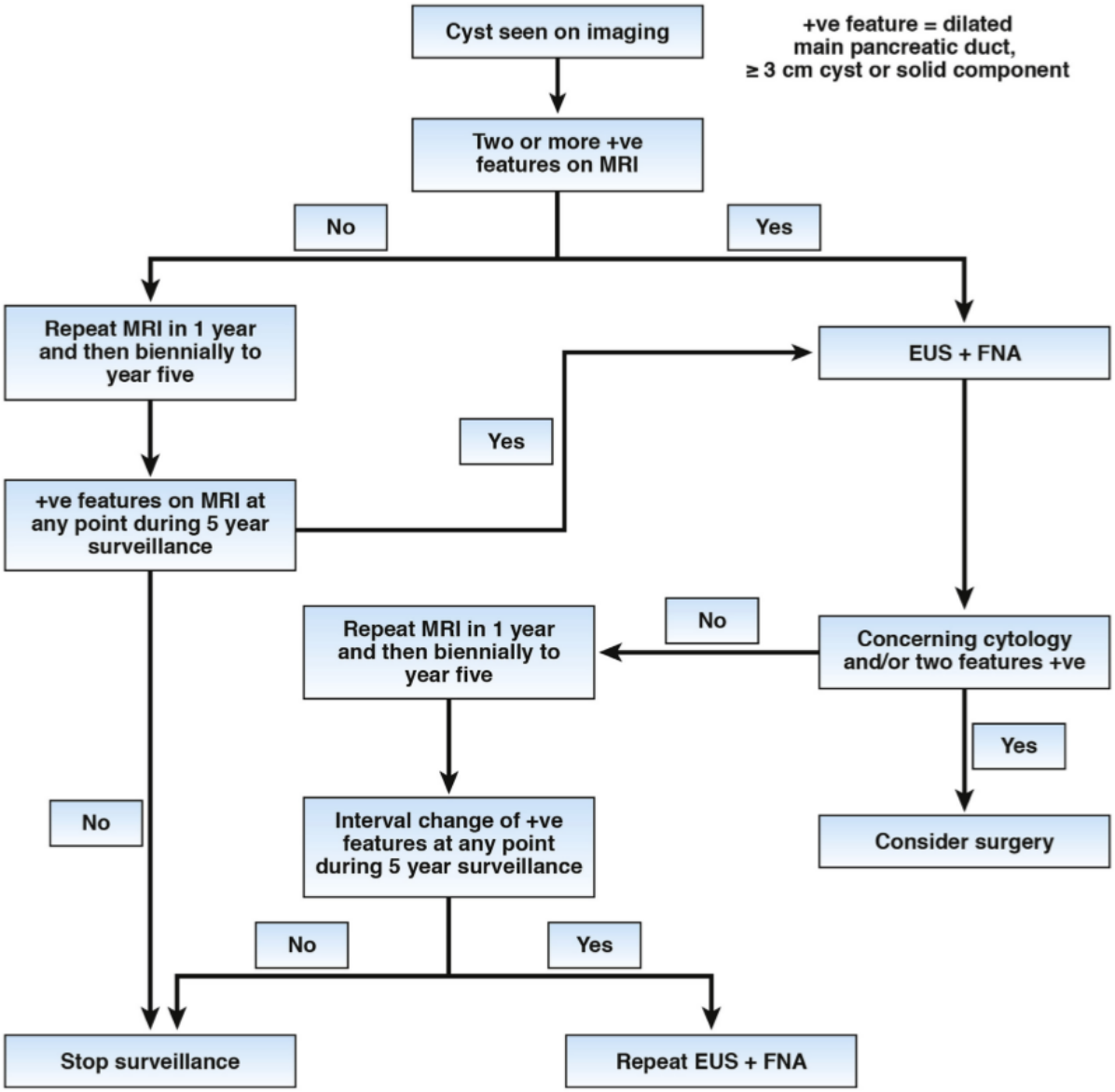
Surveillance

- Lifetime risk of malignancy of a cyst without high-risk features is <1% based on population data
- Proportion of cases developing invasive malignancy is estimated at 0.24%/year (95% CI: 0.12-0.36%)

Risk of progression to malignancy is low in cysts not initially considered for surgical resection

Management of Asymptomatic Neoplastic Pancreatic Cysts

Clinical Decision Support Tool



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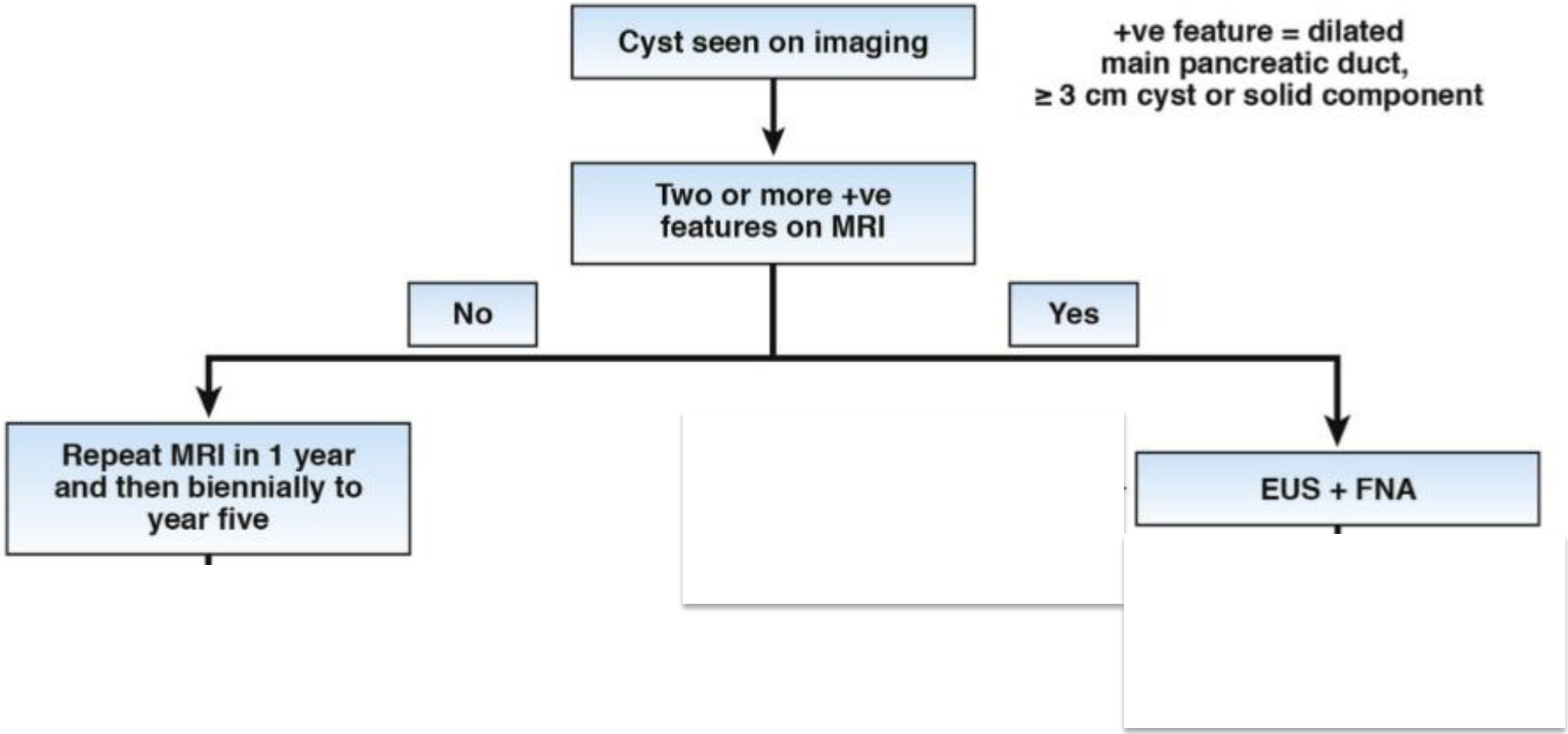
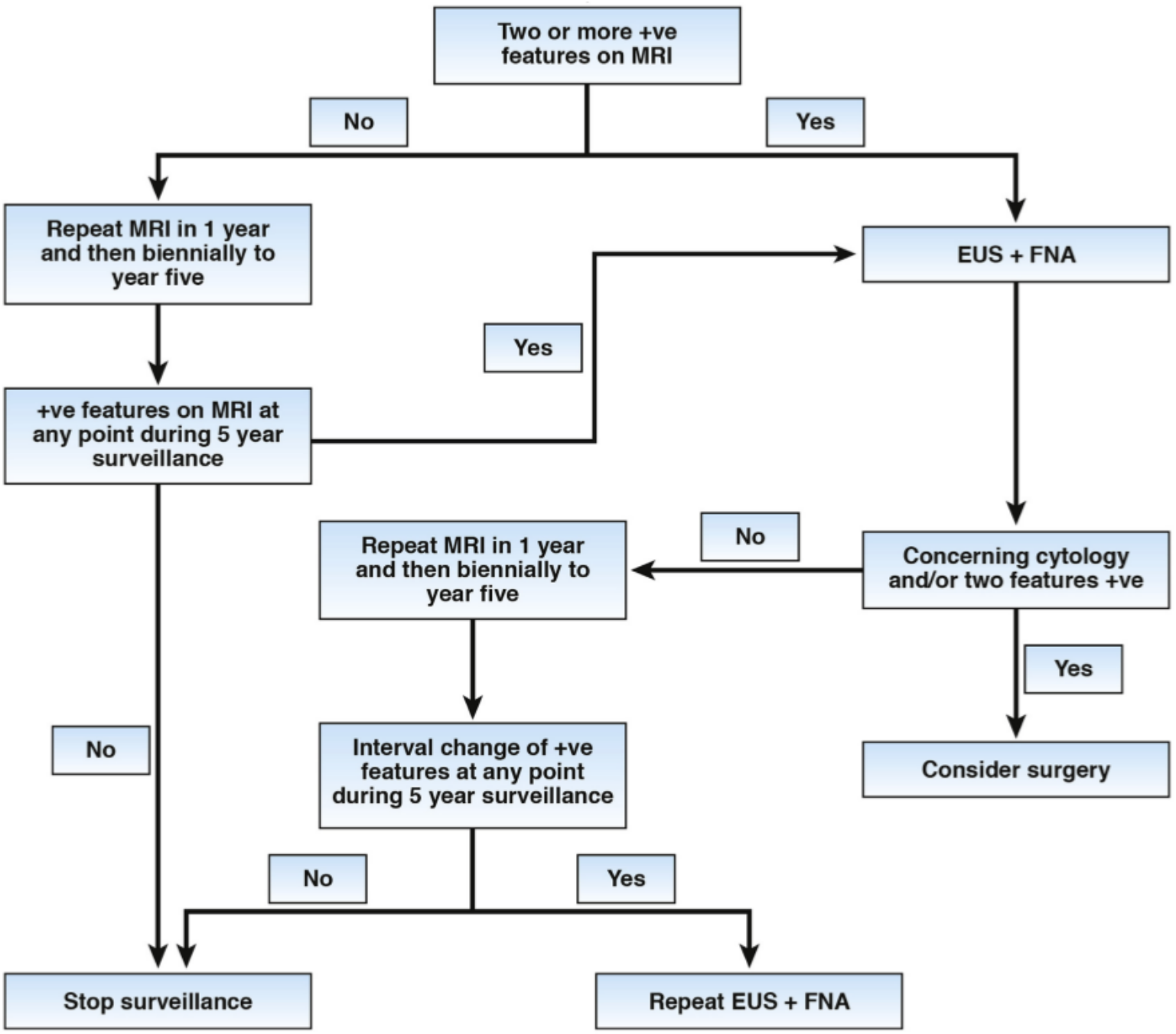



Two or more +ve features on MRI
No
Yes
Repeat MRI in 1 year and then biennially to year five
EUS + FNA
Yes
+ve features on MRI at any point during 5 year surveillance
No
Repeat MRI in 1 year and then biennially to year five
Concerning cytology and/or two features +ve
Yes
Consider surgery
No
Interval change of +ve features at any point during 5 year surveillance
No
Yes
Stop surveillance
Repeat EUS + FNA

AGA vs Sendai

Cysts <3 cm without “worrisome” features

AGA	Sendai
Cysts <3 cm without a solid component or dilated pancreatic duct undergo MRI for surveillance in 1 year then every 2 years for a total of **5 years** if there is no change is size or characteristics.	• < 1 cm: CT/MR in 2-3 years • 1-2 cm: CT/MR yearly x 2 years then lengthen interval if no change • 2-3 cm: EUS in 3-6 mo, then lengthen interval alternating MRI with EUS. Consider surgery in young, fit patients. *No recommendations regarding discontinuing surveillance*
Conditional Recommendation *Very low quality evidence*	

AGA vs Sendai

Cysts with “worrisome” features

AGA	Sendai
Cysts with at least 2 high-risk features, such as: •Size ≥3 cm •Dilated main PD •Solid component should be examined with EUS-FNA.	Cysts with worrisome features: •Pancreatitis •size ≥3 cm •Thickened/enhancing cyst wall •Non-enhancing mural nodule •Dilated main PD should be examined with EUS.
Conditional Recommendation *Very low quality evidence*	

AGA vs Sendai

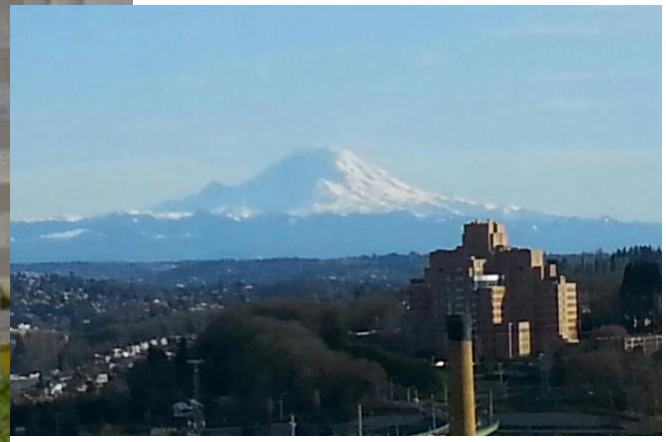
Discontinuing surveillance

AGA	Sendai
The AGA suggests against continued surveillance of pancreatic cysts if there has been no significant change in the characteristics of the cyst after 5 years of surveillance or if the patient is no longer a surgical candidate	No recommendations on discontinuation of surveillance
Conditional Recommendation *Very low quality evidence*	

Considerations

- Pancreatic cysts are common/cancer is rare
- Surveillance has potential benefits/costs
  - Annual MRI surveillance: $9.3 billion/year in US
- Treatment has potential benefits/harms
  - 15% of patients selected for surgery had cancer
  - Surgery: 2% mortality, 33% major morbidity
- Although the quality of evidence is low, there is a lot of data that can help to guide management
- Management should be individualized, guided by available data

Thank you



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