Cystic Lesions of the Pancreas

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Objectives

1. Describe clinical characteristics and pathology of common pancreatic cysts
2. Discuss advantages and disadvantages of radiology tests used
3. Provide accepted indications for operation and observation of pancreatic cysts
4. Describe role of EUS for investigation and ablation of pancreatic cysts
5. Give algorithm for management of these patients
EPIDEMIOLOGY

Epidemiology of Pancreatic Cysts

- Increasingly recognized with routine use of cross-sectional imaging
- Recent MRI\textsuperscript{1,2} and CT studies\textsuperscript{3} indicate a prevalence ranging between 2.4-14%.

Classification of Pancreatic Cysts by Cyst Lining

- **No lining**: Pseudocyst
- **Mucinous**: MCN, IPMN
- **Serous**: SCN, VHL
- **Squamous**: Lymphoepithelial cyst
- **Acinar**: Acinar cell carcinoma
- **Solid tumor degeneration**: Lymphangioma, Neuroendocrine, Sarcoma, SPT, PDAC, Pancreatoblastoma

Garcea G. Pancreatology 2008;8:236-51
Morphology of Pancreatic Cysts by Surgical Diagnosis

### Unilocular Cyst
- Pseudocyst
- Retention cyst
- IPMN
- MCN
- SCA

### Microcystic Cyst
- SCA
- IPMN

### Macrocytic Cyst
- MCN
- IPMN
- SCA
- Acinar Cystadenoma
- Lymphangioma
- Lymphoepithelial

### Cyst w/ Solid Component
- MCN
- IPMN
- SPT
- PET
- Acinar cell
- Adenocarcinoma
- Metastasis

Pittman M. Cancer Cytopathology 2010;118:1-13

Pathology Classification

### Non-Mucinous
- **Serous Neoplasms**
  - Serous cystadenoma
    - Microcystic
    - Macrocytic
    - Solid
    - Von-Hippel-Landau
  - Serous Cystadenocarcinoma

### Mucinous
- **Mucinous cystic neoplasms**
  - LGD (adenoma)
  - Moderate dysplasia (borderline)
  - HGD (carcinoma in situ)
  - Invasive carcinoma
- **IPMNs**
  - LGD (adenoma)
  - Moderate dysplasia (borderline)
  - HGD (carcinoma in situ)
  - Invasive carcinoma


### CLINICAL FEATURES

#### Clinical and Imaging Features of Common Pancreatic Cysts

<table>
<thead>
<tr>
<th></th>
<th>IPMN</th>
<th>MCN</th>
<th>SCNs</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Gender</strong></td>
<td>M = F</td>
<td>F &gt; M</td>
<td>F &gt; M</td>
</tr>
<tr>
<td><strong>Age</strong></td>
<td>60s-70s</td>
<td>40s-60s</td>
<td>60s-70s</td>
</tr>
<tr>
<td><strong>Imaging features</strong></td>
<td>Dilated main PD or side branches.</td>
<td>Unilocular; septations or peripheral CA++ rare</td>
<td>Microcysts, Central CA++, Macrocytic Variant</td>
</tr>
<tr>
<td><strong>Location</strong></td>
<td>Head, Uncinate</td>
<td>Body, Tail</td>
<td>Body, Tail</td>
</tr>
<tr>
<td><strong>Pathology</strong></td>
<td>Papillary mucinous epithelial cells without ovarian stroma</td>
<td>Mucinous epithelial cells with ovarian stroma</td>
<td>Cuboidal, glycogen-rich epithelial cells</td>
</tr>
</tbody>
</table>
Imaging of Intraductal Papillary Mucinous Neoplasm

Pathology of IPMN
Pathology of SCN

Clinical and Imaging Features of Other Pancreatic Cysts

- Pseudocyst
  - History and previous imaging consistent with pancreatitis
  - Thick wall, no septations, variable necrosis
- SPT
  - Solid and cystic mass in young woman
- PET
  - Nonfunctional tumor with cystic or mixed solid/cystic features
- Adenocarcinoma
  - Weight loss, jaundice, back pain, anorexia
  - Mostly solid
- Metastases
  - History of known malignancy, i.e. lung, melanoma, renal, colon
Questions pertaining to the Clinical Diagnosis of Pancreatic Cysts

• Clinical questions
  – Mucinous vs. Non-Mucinous
  – Benign vs. Pre-malignant vs. Malignant

• Imaging/Testing Questions
  – Imaging alone (CT, EUS, MRI)
  – Imaging + something else (CT/PET, SS-MRCP)
  – Minimally Invasive test (EUS, ERCP)
  – Minimally invasive test + something else (ERCP with pancreatography/IDUS, EUS-FNA)
  – Surgery

ABDOMINAL IMAGING
What’s the diagnosis?

MCN

MCN

SCA

PC SPT

State of the art CT

• Permits high quality CT image reformations in all three planes\(^1\)
• Increases detection of small pancreatic cystic lesions, small nodules and tumor enhancement\(^2\)
• Improves characterization of malignant potential\(^3\)

2. Sahani DV et al. Radiology 2006;238:560-9
Detection of Mural Nodules

MD IPMN

Cystic PET

Reformatted images

Main Duct IPMN

Solid Pseudopapillary Tumor
State of the art MRI

- Improvement in technology\(^1\)
  - faster breath-hold techniques
  - reduced motion artifact
- 3D MRCP
  - 2-4 mm contiguous sections through the biliary and pancreatic ducts
  - better visualization of cyst – PD communication\(^2,3\)


State of the art MRI

- Secretin MRCP improves the visualization of PD and tumor-to-PD communication\(^1\)
- Soft-tissue contrast improves depiction of the septa and internal contents of pancreatic cysts\(^2,3,4\)

4. Macari M. Radiology 2009;251:77-84
Imaging Studies

• CT and MRI
  – 40-60% accurate for predicting the correct histologic diagnosis
  – 70-90% accurate in differentiating nonaggressive versus aggressive lesions

• Increasing concern with repeated imaging
  – 1.5-2% of cancers in the U.S. are related to radiation from CT scans

Procacci et al, J Comput Assist Tomog 1999,
Sainani et al, Am J Roent 2009,
Visser et al, Am J Roent 2007,
Ogawa et al, Radiology 2008;
Brenner et al, NEJM 2007
Classic pictures

EUS FNA pancreatic cyst
### EUS-FNA and Cyst Fluid Analysis of Cystic Pancreatic Lesions

<table>
<thead>
<tr>
<th>Lesion</th>
<th>Fluid Color</th>
<th>Viscosity</th>
<th>CEA</th>
<th>Amylase</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudocyst</td>
<td>Yellow/brown</td>
<td>Thin</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>SCN</td>
<td>Colorless</td>
<td>Thin</td>
<td>Low/Undetected</td>
<td>Variable</td>
</tr>
<tr>
<td>MCN</td>
<td>Colorless</td>
<td>Usually thick</td>
<td>++</td>
<td>Variable</td>
</tr>
<tr>
<td>MCAC</td>
<td>Colorless</td>
<td>Thick</td>
<td>+++</td>
<td>Variable</td>
</tr>
<tr>
<td>IPMN</td>
<td>Colorless</td>
<td>Usually thick</td>
<td>+ to +++</td>
<td>High</td>
</tr>
</tbody>
</table>

### EUS-FNA of pancreatic cyst

- Cyst fluid CEA 192 ng/mL optimizes non-MCN vs. MCN\(^1\)
- Cyst fluid cytology is insensitive but very specific for diagnosis, malignancy and MCN vs. non-MCN\(^2\)
- Cyst fluid DNA may help differentiate malignant/benign and mucinous vs. non-mucinous cysts\(^3\)

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1. Brugge WR. Gastroenterology 2004; 126:1330-6
WHEN TO OPERATE?

Risk of Invasive Malignancy in Mucinous Cystic Tumors

- Main Duct IPMNs: 30-50%
- Mucinous Cystic Neoplasms: 10-20%
- BD-IPMNs: 10-20%
- Referral bias in surgical series clearly overstates true malignancy risk

Le Borgne J. Ann Surg 1999
Kiely JM. J Gastrointest Surg 2003
Sohn TA. Ann Surg 2004
Spinelli KS. Ann Surg 2004
Rodriguez JR. Gastroenterology 2007
Allen PJ. Ann Surg 2006
### Morbidity and Mortality in Surgical Series for Pancreatic Cysts

<table>
<thead>
<tr>
<th>Author, yr</th>
<th>N</th>
<th>Morbidity</th>
<th>Mortality</th>
<th>LOS</th>
<th>Comments</th>
</tr>
</thead>
<tbody>
<tr>
<td>Le Borgne, 1999</td>
<td>372</td>
<td>-</td>
<td>1.4-7%</td>
<td>-</td>
<td>Diff types of cysts</td>
</tr>
<tr>
<td>Kiley, 2003</td>
<td>30</td>
<td>20-33%</td>
<td>2%</td>
<td>13</td>
<td>Diff types of cysts</td>
</tr>
<tr>
<td>Sohn, 2004</td>
<td>136</td>
<td>35%</td>
<td>3.7%</td>
<td>-</td>
<td>Only IPMNs</td>
</tr>
<tr>
<td>Spinelli, 2004</td>
<td>49</td>
<td>20-36%</td>
<td>2%</td>
<td>13</td>
<td>Diff types of cysts</td>
</tr>
<tr>
<td>Allen, 2006</td>
<td>170</td>
<td>22%</td>
<td>0.6%</td>
<td>-</td>
<td>Diff types of cysts</td>
</tr>
<tr>
<td>Rodriguez, 2007</td>
<td>145</td>
<td>27%</td>
<td>0%</td>
<td>9</td>
<td>Only BD-IPMNs</td>
</tr>
<tr>
<td>Schmidt, 2007</td>
<td>156</td>
<td>31%</td>
<td>2.5%</td>
<td>-</td>
<td>Only IPMNs</td>
</tr>
</tbody>
</table>

Le Borgne J. Ann Surg 1999  
Kiley JM. J Gastrointest Surg 2003  
Sohn TA. Ann Surg 2004  
Spinelli KS. Ann Surg 2004  
Rodriguez JR. Gastroenterology 2007  
Schmidt M. Ann Surg 2007  

### Natural History of BD-IPMNs

<table>
<thead>
<tr>
<th>Author/ Yr</th>
<th>Design</th>
<th>N</th>
<th>F/U (mos)</th>
<th>↑ Size</th>
<th>Mural Nodule</th>
<th>MPD change</th>
<th>CBD dilation</th>
</tr>
</thead>
<tbody>
<tr>
<td>Irie ‘04</td>
<td>P</td>
<td>29</td>
<td>≥12</td>
<td>3%</td>
<td>-</td>
<td>0%</td>
<td>-</td>
</tr>
<tr>
<td>Kobayashi, ‘05</td>
<td>R</td>
<td>47</td>
<td>41</td>
<td>2%</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Levy, ‘06</td>
<td>R</td>
<td>32</td>
<td>60</td>
<td>0%</td>
<td>0%</td>
<td>0%</td>
<td>NR</td>
</tr>
<tr>
<td>Carbognin, ‘06</td>
<td>P</td>
<td>36</td>
<td>27</td>
<td>6%</td>
<td>0%</td>
<td>0%</td>
<td>NR</td>
</tr>
<tr>
<td>Lee ‘07</td>
<td>R</td>
<td>45</td>
<td>27</td>
<td>22%</td>
<td>-</td>
<td>-</td>
<td>-</td>
</tr>
<tr>
<td>Salvia ‘07</td>
<td>P</td>
<td>89</td>
<td>32</td>
<td>5%</td>
<td>NR</td>
<td>NR</td>
<td>NR</td>
</tr>
<tr>
<td>Tanno ‘08</td>
<td>P</td>
<td>82</td>
<td>61</td>
<td>11%</td>
<td>4.9%</td>
<td>0%</td>
<td>NR</td>
</tr>
<tr>
<td>Rautou, ‘08</td>
<td>P</td>
<td>121</td>
<td>33</td>
<td>25%</td>
<td>2.5%</td>
<td>4.1%</td>
<td>2.5%</td>
</tr>
</tbody>
</table>

Kobayashi G. J. Gastroenterol 2005  
Irie H. J Comput Assist Tomogr. 2004  
Lee SH. Kor J Gastroenterol 2007  
Carbognin G. Abd Imaging 2006  
Levy PL. CGH 2006  
Rautou PE. CGH 2008  
Salvia R. Gut 2007  
Tanno S. Gut 2008
MD-IPMN

- Indication for resection
  - All surgically fit patients
    - Related to high incidence of malignant/invasive lesions and low 5 year survival rates

Tanaka et al, Pancreatology 2012

MCN

- Indication for resection
  - All surgically fit patients
    - Related to relatively young age of patients, usual location in pancreatic body/tail and risk of progression as well as need for long term surveillance due to malignant potential

Tanaka et al, Pancreatology 2012
### BD-IPMN 2012 Guidelines

**Are any of the following high-risk features of malignancy present?**
- Jaundice
- whitish color of the stool
- a main pancreatic duct >10 mm in size

### Is cyst ablation indicated?**
- Additional cystic fluid analysis
- CT or MRI

### Are any of the following worrisome features present?**
- Imaging: i) cyst >5 cm, ii) thickened/enhancing cyst walls, iii) main duct size >10 mm
- Non-enhancing internal nodular or papillary change in caliber of pancreatic duct with dilated pancreatic duct

### Are any of these features present?**
- Ductal intraductal papillary neoplasm
- Cytology: suspicious or consistent with malignancy

<table>
<thead>
<tr>
<th>Size of Target Cyst</th>
<th>Management</th>
</tr>
</thead>
</table>
| <1 cm               | Close surveillance alternating 6-12 months, with EUS in 6-12 months. |<-
| 1-2 cm              | Close surveillance alternating 6-12 months, with EUS in 6-12 months. |<-
| 3-5 cm              | Close surveillance alternating 6-12 months, with EUS in 6-12 months. |<-
| >5 cm               | Close surveillance alternating 6-12 months, with EUS in 6-12 months. |<-

*Tanaka et al, Pancreatology 2012*
EUS-guided cyst ablation

- EUS-FNI ethanol
- ↓ viable epithelium
- smaller size
- Time and follow up imaging
- Cyst resolution

EUS-guided ethanol lavage

- Ethanol lavage: resolution of about 1/3\(^1,2\)
- Ethanol and paclitaxel: resolution or near resolution in up to 2/3\(^3,4\)
- Abdominal pain in 10%
- Pancreatitis in 1-10%
- Histologic ablation
- Long term resolution

2. DeWitt J. GIE 2009;70:710-23
3. Oh HC. Gastroenterology 2011;140:172-9
Baseline CT and EUS at IUMC in December 2008

- 2.7 cm cyst in HOP
- Cyst CEA>1000.
- Cytology: NACI
  - DNA quantity: Moderate
  - DNA quality: Poor
- KRAS mutation: None
- Allelic imbalance (LOH): none
EUS FNI #1 Jan 2009

EUS-FNA and EUS-FNI #2 in April 2009

EUS 3 months later.
15 x 8 mm cyst with 3.5 mm wall and mural calcifications
EUS-FNA and EUS-FNI #2 in April 2009

Reinjected with ethanol and paclitaxel.

CT in October 2009 – 6 months after 2\textsuperscript{nd} injection

Complete Resolution (1\% orig. volume) by CT after 2\textsuperscript{nd} injection
Conclusion

- Pancreatic cysts
  - are increasingly recognized with routine use of cross-sectional imaging
  - may be classified by multiple methods (path, morphology, cell of origin, etc.)
  - have characteristic but not universal imaging and demographic characteristics
Conclusion

• MDCT and MRI/MRCP
  – Similar at determining cyst “aggressiveness” and malignancy
  – Neither accurate at determining diagnosis
  – Best to tailor test to probable diagnosis

Conclusion

• EUS
  – Morphology alone inaccurate except for microcystic SCN
  – Cyst fluid cytology insensitive but specific
  – Cyst fluid CEA most accurate tumor marker
  – DNA analysis may increase diagnostic yield but prognostic information unknown
Conclusions

• Surgery for pancreatic cysts is associated with frequent morbidity and rare mortality
• Recommended for MD-IPMN, MCN, BD-IPMN with high risk features
• Cysts monitored under surveillance or discovered in high risk patients may present opportunity to intervene nonoperatively

Conclusions

• Endoscopic ablation of pancreatic cysts
  – leads to varying degrees of pathologic epithelial ablation and radiologic regression
  – is associated with partial or complete radiologic regression in the majority
  – persistent radiologic resolution to date
  – complicated by acute pancreatitis in 5-10%