Pancreatic Cyst Epidemiology

- Autopsy data suggests 25% pancreata contain a cyst
- Prevalence of incidental pancreatic cysts in the adult population on MR imaging (Lee et al. Amer J Gastro 2010)
## Type of pancreatic cysts

(Law et al. 2013 Current opinion in gastro)

<table>
<thead>
<tr>
<th>No Malignant Potential</th>
<th>Malignant Potential</th>
<th>Malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pseudocyst</td>
<td>Intraductal papillary mucinous neoplasm</td>
<td>Cystic ductal adenocarcinoma</td>
</tr>
<tr>
<td>Serous cystic adenoma</td>
<td>Mucinous cystic neoplasm</td>
<td>Cystic neuroendocrine tumor</td>
</tr>
<tr>
<td>Retention Cyst</td>
<td>Intraductal tubular carcinoma</td>
<td>Solid pseudopapillary neoplasm</td>
</tr>
<tr>
<td>Congenital Cyst</td>
<td></td>
<td>Cystic pancreatoblastoma</td>
</tr>
<tr>
<td>Endometrial cyst</td>
<td></td>
<td>Cystic acinar cystadenocarcinoma</td>
</tr>
<tr>
<td>Cystic lymphangioma</td>
<td></td>
<td>Mature cystic teratoma</td>
</tr>
<tr>
<td>Cavernous hemangioma</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Lymphoepithelial cyst</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

## Calculation of pancreatic cyst prevalence in the US population in adults between age 40 and 84

(Gardner et al. Oct 2013 American Journal of Gastro)

<table>
<thead>
<tr>
<th>Age Group</th>
<th>US Population</th>
<th>Cyst Prevalence Rate (%)</th>
<th>Total Number of Cysts</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total population</td>
<td>137,154,960</td>
<td>2.5</td>
<td>3,428,874</td>
</tr>
<tr>
<td>40–49-year-olds</td>
<td>43,599,555</td>
<td>1.35</td>
<td>588,594</td>
</tr>
<tr>
<td>50–59-year-olds</td>
<td>41,962,930</td>
<td>2.05</td>
<td>860,240</td>
</tr>
<tr>
<td>60–69-year-olds</td>
<td>29,253,187</td>
<td>3.25</td>
<td>950,729</td>
</tr>
<tr>
<td>70–79-year-olds</td>
<td>16,595,961</td>
<td>7.3</td>
<td>1,211,505</td>
</tr>
<tr>
<td>80–84-year-olds</td>
<td>5,743,327</td>
<td>8.7</td>
<td>499,669</td>
</tr>
</tbody>
</table>

a US population determined from 2010 United States census information
b The cyst prevalence rate was determined by combining the mean cyst rate of the two most scientifically rigorous cross-sectional imaging studies on cyst prevalence
Patient #4

- Serous Cystadenoma
- IPMN with high-grade dysplasia
- IPMN with low-grade dysplasia
- IPMN with microinvasive CA
What Do We Need?

- Which cyst will never get cancer? (Forget)
  - Mucinous vs. Non-mucinous cysts
- Which cyst has invasive cancer/HGD currently or will develop it in a short-period of time? (Resect)
- Which cyst will develop HGD or invasive cancer in the future years? (Surveillance)

### Diagnostic features of Most Common Pancreatic Cystic Lesions (adapted from Fasanella et al. Best Prac Res Clin Gastroenterology 2009)

<table>
<thead>
<tr>
<th>Cyst type</th>
<th>EUS features</th>
<th>Fluid appearance</th>
<th>Cytology</th>
<th>CEA</th>
<th>Amylase</th>
<th>Mutation Status</th>
</tr>
</thead>
<tbody>
<tr>
<td>SCA</td>
<td>Microcystic, honeycombed, 20% macrocystic</td>
<td>Thin, clear, sometimes bloody</td>
<td>Cuboidal cells, clear glycogen-positive cytoplasm Mucin-rich fluid, columnar mucin-positive cells, variable atypia</td>
<td>Low</td>
<td>Low</td>
<td>VHL</td>
</tr>
<tr>
<td>MCN</td>
<td>Macrocystic</td>
<td>Viscous, clear</td>
<td>Mucin-rich fluid, columnar mucin-positive cells, variable atypia</td>
<td>High</td>
<td>Low</td>
<td>KRAS</td>
</tr>
<tr>
<td>IPMN</td>
<td>Cystic branch duct dilation, dilated main PD</td>
<td>Viscous, clear</td>
<td>Inflammatory cells without evidence of mucin or epithelial cells</td>
<td>High</td>
<td>High</td>
<td>KRAS/GNAS</td>
</tr>
<tr>
<td>PP</td>
<td>Macrocytic, thick wall, unilocular, internal debris</td>
<td>Thin, dark, non-mucinous</td>
<td></td>
<td>Variable</td>
<td>High</td>
<td></td>
</tr>
</tbody>
</table>
### Diagnostic Features of Pancreatic Cystic Lesions

<table>
<thead>
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</tr>
</thead>
<tbody>
<tr>
<td>Cystic PET</td>
<td>Variable</td>
<td>Variable, typically non-mucinous</td>
<td>Small cells, scant cytoplasm, monomorphic nuclei, Papillary structures, macrophages, myxoid stroma, monomorphic neoplastic cells</td>
<td>Unknown</td>
<td>Low</td>
</tr>
<tr>
<td>SPT</td>
<td>Mixed solid and cystic</td>
<td>Bloody</td>
<td></td>
<td>Low</td>
<td>Low</td>
</tr>
<tr>
<td>LEC</td>
<td>Solid, heterogeneous, subtle posterior enhancement</td>
<td>Thick milky, gray or frothy</td>
<td>Anucleated squamous cells, lymphocytes</td>
<td>Variable</td>
<td>Low</td>
</tr>
</tbody>
</table>

(adapted from Fasanella et al. Best Prac Res Clin Gastroenterology 2009)

### Clinical Factors that Guide Management of the Cysts

- Age of patient
- Co-morbid conditions
- Location of cyst
- Size of cyst
- Multi-focal vs. solitary
- Associated risk factors: Family history, h/o pancreatitis
- Symptoms
- Risk for cancer development

<table>
<thead>
<tr>
<th>Feature</th>
<th>Odds Ratio (Confidence Interval)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cyst size greater than 3 cm</td>
<td>62.4 (30.8 – 126.3)</td>
</tr>
<tr>
<td>Presence of a mural nodule</td>
<td>9.3 (5.3 – 16.1)</td>
</tr>
<tr>
<td>Dilatation of the MPD</td>
<td>7.3 (3.0 – 17.4)</td>
</tr>
<tr>
<td>Main vs Branch Duct IPMN</td>
<td>4.7 (3.3 – 6.9)</td>
</tr>
<tr>
<td>Symptoms (not usually specified in the studies)</td>
<td>1.6 (1.0 – 26)</td>
</tr>
</tbody>
</table>

## Degree of Dysplasia Based on Cyst Size
(Sahora et al. Annals of Surgery 2013)
Worrisome features present?

- Clinical: pancreatitis
- Imaging:
  - cyst > 3 cm
  - thickened/enhancing cyst walls
  - Main-duct size 5-9 mm
  - Non-enhancing mural nodule
  - Abrupt change in caliber of pancreatic duct with distal pancreatic atrophy

Pancreatology, Volume 12, Issue 3 2012 183 - 197
Predicting Dysplasia and Invasive Carcinoma in IPMN: Study Cohort (Currea-Gallego et al. Ann Surg Onc 2013)

Resected IPMN
n = 283

IPMN
n = 219

Branch duct
56%

Main & mixed
44%

Benign
70%

HGD
15%

Invasive
15%

Benign
26%

HGD
33%

Invasive
41%

64 Excluded
No available cross sectional imaging

Predicting Dysplasia and Invasive Carcinoma in IPMN: Study Cohort (Currea-Gallego et al. Ann Surg Onc 2013)
Risk of pancreatic cancer in IPMNs- Field defect?

Bartsch et al. Fam Cancer 2013

Baseline EUS December 2009
Metachronous PDAC in Region Separate from the Index Cyst

<table>
<thead>
<tr>
<th>Study</th>
<th>n</th>
<th>Diagnosis to PDAC (months)</th>
<th>Risk of metachronous PDAC in separate region N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tada et al. 2006</td>
<td>80</td>
<td>48</td>
<td>2 (2.5%)</td>
</tr>
<tr>
<td>Uehara et al. 2008</td>
<td>60</td>
<td>87</td>
<td>5 (8.0%)</td>
</tr>
<tr>
<td>Tanno et al. 2010</td>
<td>168</td>
<td>NS</td>
<td>4 (2.4%)</td>
</tr>
<tr>
<td>Ingkakul et al. 2010</td>
<td>236</td>
<td>NS</td>
<td>2 (0.8%)</td>
</tr>
<tr>
<td>LaFemina et al. 2013</td>
<td>170</td>
<td>NS</td>
<td>10 (2.8%)</td>
</tr>
</tbody>
</table>
High-risk stigmata of malignancy present?

- Obstructive jaundice in a cystic lesion of the head of the pancreas
- Enhancing solid component within cyst
- Main pancreatic duct $>10$ mm in size

If yes to any of the above should consider surgery if clinically appropriate.
If no, look for presence of worrisome features
Worrisome features present?

- Clinical: pancreatitis
- Imaging:
  - cyst $\geq$ 3 cm
  - thickened/enhancing cyst walls
  - Main-duct size 5-9 mm
  - Non-enhancing mural nodule
  - Abrupt change in caliber of pancreatic duct with distal pancreatic atrophy

If any features present perform EUS looking for:

1. Definite mural nodule
2. Main duct features suspicious for involvement
3. Cytology suspicious or positive for malignancy

If no worrisome or high-risk features present in cyst need to determine size of largest cyst

- < 1 cm
  - CT/MRI in 2-3 years

- 2-3 cm
  - EUS in 3 to 6 months, then lengthen interval alternating with MRI with EUS as appropriate

- 1-2 cm
  - CT/MRI yearly x 2 years then lengthen interval in no change

- > 3 cm
  - Close surveillance alternating MRI with EUS every 3 to 6 months, strongly consider surgery in young, fit patients
Summary

• Presently would follow 2012 Guidelines
• Even if you resect an IPMN, one must continue to do surveillance
• Future work focused on:
  – Defining those cysts that currently have HGD or invasive cancer or will develop it during their lifetime
  – Most cost-effective manner of doing surveillance