IPMN and PanIn: Recognizing Precancerous Lesions of the Pancreas

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Professor and Chief, Gastroenterology
Endowed Chair, GI Endoscopic Oncology

UC Irvine Health
Case: Pancreatic Cyst

- 65 yo female was found to have an incidental 2.9 cm cyst in the head of the pancreas
Case: Pancreatic Cyst

Q 1: What would you do next?

1. Whipple resection
2. Repeat CT in 12 months
3. MRI/MRCP
4. ERCP
5. EUS/FNA
Case: High Risk Family History

- 49 yo asymptomatic male, with family history of pancreatic cancer (father and brother)
- Ca19-9 normal
- CT of abdomen normal
Case: Familial Pancreas Cancer

Q 2: What would you do next?

1. Whipple resection
2. Repeat CT in 12 months
3. MRI/MRCP
4. ERCP
5. EUS/FNA
Outline

- Recognizing IPMN
- Risk stratification of IPMN
- Algorithm for Panc Cyst
- When to suspect PanIn
- Work-up for PanIn
### Pathology Classification

<table>
<thead>
<tr>
<th>Non-Mucinous</th>
<th>Mucinous</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Serous Neoplasms</strong></td>
<td><strong>Mucinous cystic neoplasms</strong></td>
</tr>
<tr>
<td>Serous cystadenoma</td>
<td>– LGD (adenoma)</td>
</tr>
<tr>
<td>Microcystic</td>
<td>– Moderate dysplasia (borderline)</td>
</tr>
<tr>
<td>Macrocystic</td>
<td>– HGD (carcinoma in situ)</td>
</tr>
<tr>
<td>Solid</td>
<td>– Invasive carcinoma</td>
</tr>
<tr>
<td>Von-Hippel-Landau</td>
<td></td>
</tr>
<tr>
<td>Serous Cystadenocarcinoma</td>
<td></td>
</tr>
<tr>
<td></td>
<td><strong>IPMNs</strong></td>
</tr>
<tr>
<td></td>
<td>– LGD (adenoma)</td>
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<td>– Invasive carcinoma</td>
</tr>
</tbody>
</table>


Serous Cystadenoma/ Microcystic Adenoma
Mucinous Cystic Neoplasm (MCN)
Intraductal Papillary Mucinous Neoplasia (IPMN)
IPMN – Main Duct Type
IPMN – Endoscopic View
Tanaka et al. Pancreatology 2006

Main Duct IPMN

Older Patients

- Arise within the head and progress distally
- >1cm Main PD strongly suggests MD-IPMN
- Higher risk of malignancy (57% - 92%)
- Resect

Branched Duct IPMN

Younger Patients

- Arise in the uncinate process & tail
- Cyst communicating with PD without Main duct dilation suggests BD-IPMN
- Lower risk of malignancy (6% - 42%)
- Monitor vs Resect
Sendai Consensus Guidelines 2004

Risk Factors:

- Size > 3cm
- High risk features
  - Mural nodules
  - Dilated main PD (> 10mm)
  - Positive Cytology
Mural nodules
Updated “Sendai” Guidelines 2012

**Are any of the following high-risk stigmata of malignancy present?**
- i) obstructive jaundice in a patient with cystic lesion of the head of the pancreas,
- ii) enhancing solid component within cyst,
- iii) main pancreatic duct ≥10 mm in size

**Yes**
- Consider surgery, if clinically appropriate

**No**
- **Are any of the following worrisome features present?**
  - **Clinical:** Pancreatitis
  - **Imaging:** i) cyst ≥3 cm, ii) thickened/enhancing cyst walls, iii) main duct size 5-9 mm, iv) non-enhancing mural nodule, v) abrupt change in caliber of pancreatic duct with distal pancreatic atrophy.

  - **If yes, perform endoscopic ultrasound**

**Are any of these features present?**
- i) Definite mural nodule(s)
- ii) Main duct features suspicious for involvement
- iii) Cytology: suspicious or positive for malignancy

**Yes**
- **<1 cm**
  - CT/MRI in 2-3 years
- **1-2 cm**
  - CT/MRI yearly x 2 years, then lengthen interval if no change
- **2-3 cm**
  - EUS in 3-6 months, then lengthen interval alternating MRI with EUS as appropriate.
  - Consider surgery in young, fit patients with need for prolonged surveillance
- **>3 cm**
  - Close surveillance alternating MRI with EUS every 3-6 months. Strongly consider surgery in young, fit patients

**No**
- **Inconclusive**
  - What is the size of largest cyst?
  - **<1 cm**
    - CT/MRI in 2-3 years
  - **1-2 cm**
    - CT/MRI yearly x 2 years, then lengthen interval if no change
  - **2-3 cm**
    - EUS in 3-6 months, then lengthen interval alternating MRI with EUS as appropriate.
    - Consider surgery in young, fit patients with need for prolonged surveillance
  - **>3 cm**
    - Close surveillance alternating MRI with EUS every 3-6 months. Strongly consider surgery in young, fit patients
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>
CEA from Pancreatic Cyst

- Cyst fluid CEA 192 ng/mL optimizes non-MCN vs. MCN\(^1\)

1. Brugge WR. Gastroenterology 2004; 126:1330-6
6 months later, a repeat EUS shows no change in size or morphology, but the CEA level went from 168 to 550
Q 3: Now what?

1. Whipple resection
2. Repeat CT in 12 months
3. MRI/MRCP in 3 months
4. ERCP
5. Repeat EUS/FNA in 6 months
Limitations of CEA

- Although may help distinguish mucinous vs non-mucinous, does not distinguish IPMN vs MCN
- Not predictive of malignant progression\(^1\)
- Not predictive of cyst size progression\(^1\)
- Serial follow-up levels may be erratic\(^2\)

1. Othman MO. Dig Liver Dis 2012; 44:844-8
2. Nakai Y. ASGE abstract submission 2012
Serial CEA values in 87 patients

Nakai Y. Chang K. DDW 2012
Limitaitons of Cyst Size

- Not all small side-branch IPMN are benign, despite negative cytology
- Among 20 patients with < 3cm SB-IPMN, 6 (30%) had CIS (3) or invasive cancer (3)\(^1\)
- Cyst size > 3cm (*Sendai Guideline*) NOT a predictor of malignancy among 112 surgical cases\(^2\)

1. Pitman MB. Pancreatology 2008;8;277-85
Limitation of Imaging Morphology

Even Surgical Morphology overlaps

**Unilocular**
- Pseudocyst
- Retention cyst
- IPMN
- MCN
- SCA

**Microcystic**
- SCA
- IPMN

**Macrocystic**
- MCN
- IPMN
- SCA
- Acinar cell
- Cystadenoma
- Lymphangiomia
- Lymphoepithelial

**Cyst w/ solid component**
- MCN
- IPMN
- SPT
- PET
- Adenocarcinoma
- Metastasis
- Acinar cell

Pittman M. Cancer Cytopathology 2010; 118:1-13
Table 3. DNA Analysis of Pancreatic Cyst Fluid Can Identify Patterns of Genetic Alterations that Define Cyst Type

<table>
<thead>
<tr>
<th>Variable</th>
<th>KRAS</th>
<th>GNAS</th>
<th>RNF43</th>
<th>CTNNB1</th>
<th>VHL</th>
</tr>
</thead>
<tbody>
<tr>
<td>IPMN</td>
<td>+</td>
<td>+</td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>MCN</td>
<td>+</td>
<td></td>
<td>+</td>
<td></td>
<td></td>
</tr>
<tr>
<td>SPN</td>
<td></td>
<td></td>
<td></td>
<td>+</td>
<td></td>
</tr>
<tr>
<td>SCA</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td>+</td>
</tr>
</tbody>
</table>

IPMN, intraductal papillary mucinous neoplasm; MCN, mucinous cystic neoplasm; SPN, solid-pseudopapillary neoplasm; SCA, serous cystadenoma.
Pancreatic Cysts: Conundrum

Imaging?

CEA?

Amylase?

Cytology?

Biomarkers?

Size?

SCA
MCN
IPMN
SPPT
The answer is on the wall…

Frossard AJG 2003

SCA

PAS+ cuboidal glycogen-staining cells

MCN

Frossard AJG 2003
The answer is on the wall…

IPMN
Cytology

- Yield of cytology is low
- Usually cannot distinguish MCN vs IPMN
- May not distinguish grade of dysplasia, which also may require histology
- Cannot distinguish IPMN histologic subtype

1. Furakawa T. Gut 2011; 60:509-16
You are now fairly sure that the patient has IPMN
Q 4: Which is most predictive of progression to cancer?

1. Male sex
2. Size of cyst
3. Main Duct type vs Side branch type
4. IPMN histologic subtype
5. CEA level
IPMN - 4 Histologic Types

- Gastric type, adenoma
- Intestinal type, borderline neoplasms
- Pancreatobiliary type, carcinoma
- Oncocytic type, carcinoma

Yamaguchi, H. Modern Pathology 2007;20, 552–561
IPMN - 4 Histologic Sub-Types

283 pts with IPMN

Furukawa Gut 2011
### Table 2: Cox proportional hazards model analysis

<table>
<thead>
<tr>
<th></th>
<th>HR</th>
<th>Lower boundary</th>
<th>Upper boundary</th>
<th>p Value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>All data</strong></td>
<td></td>
<td></td>
<td></td>
<td>3.68×10⁻⁸</td>
</tr>
<tr>
<td><strong>Stage</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>0 vs 0A</td>
<td>10.907</td>
<td>1.187</td>
<td>100.192</td>
<td>0.0347</td>
</tr>
<tr>
<td>IA vs 0A</td>
<td>13.132</td>
<td>1.049</td>
<td>164.320</td>
<td>0.0458</td>
</tr>
<tr>
<td>IB vs 0A</td>
<td>75.202</td>
<td>8.237</td>
<td>686.580</td>
<td>1.29×10⁻⁴</td>
</tr>
<tr>
<td>IIA vs 0A</td>
<td>44.869</td>
<td>4.610</td>
<td>436.686</td>
<td>0.0011</td>
</tr>
<tr>
<td>IIB vs 0A</td>
<td>267.942</td>
<td>28.358</td>
<td>2531.694</td>
<td>1.07×10⁻⁶</td>
</tr>
<tr>
<td><strong>Morphological type</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.0435</td>
</tr>
<tr>
<td>GAS vs INT</td>
<td>1.957</td>
<td>0.705</td>
<td>5.436</td>
<td>0.1975</td>
</tr>
<tr>
<td>ONC vs INT</td>
<td>1.541</td>
<td>0.495</td>
<td>4.794</td>
<td>0.4556</td>
</tr>
<tr>
<td><strong>PB vs INT</strong></td>
<td>4.964</td>
<td>1.642</td>
<td>15.002</td>
<td>0.0045</td>
</tr>
<tr>
<td><strong>Macroscopic type</strong></td>
<td></td>
<td></td>
<td></td>
<td>0.1702</td>
</tr>
<tr>
<td>Mixed vs BT</td>
<td>0.947</td>
<td>0.301</td>
<td>2.983</td>
<td>0.9261</td>
</tr>
<tr>
<td>MT vs BT</td>
<td>2.109</td>
<td>0.791</td>
<td>5.623</td>
<td>0.1360</td>
</tr>
</tbody>
</table>

Furukawa Gut 2011
### Table 1: Subtype classification of IPMN by immunohistochemical analysis and arising invasive carcinoma [48–50].

<table>
<thead>
<tr>
<th>IPMN (subtype)</th>
<th>Expression profile</th>
<th>Invasive carcinoma</th>
</tr>
</thead>
<tbody>
<tr>
<td>Intestinal (MD-IPMN)</td>
<td>MUC5AC⁺, MUC2⁺, CDX-2⁺ (MUC1⁻, MUC6⁻)</td>
<td>Colloidal carcinoma</td>
</tr>
<tr>
<td>Pancreatobiliary (MD-IPMN)</td>
<td>MUC5AC⁺, MUC1⁺ (MUC2⁻, MUC6⁺⁻⁻)</td>
<td>Tubular (ductal) carcinoma</td>
</tr>
<tr>
<td>Gastric (BD-IPMN)</td>
<td>MUC5AC⁺, (MUC6⁺⁻⁻⁻) (MUC1⁻, MUC2⁻)</td>
<td>Tubular (ductal) carcinoma</td>
</tr>
<tr>
<td>Oncocytic (MD-IPMN)</td>
<td>MUC5AC⁺, MUC6⁺ (MUC2⁺⁻⁻⁻) (MUC1⁺⁻⁻⁻)</td>
<td>Oncocytic carcinoma</td>
</tr>
</tbody>
</table>
FIGURE 2. Representative images of the gastric subtype IPMN. Histology (a, c, e, g: ×200); cytology (b, d, f, h: ×400). Hematoxylin and eosin staining (A), papanicolaou staining (B), and immunostainings of MUC1 core (C, D), MUC2 (E, F), and MUC5AC (G, H).

Histologically and cytologically, the neoplastic cells expressed MUC5AC, but were negative for MUC1 core and MUC2.
FIGURE 3. Representative images of the intestinal subtype IPMN. Histology (a, c, e, g: ×200); cytology (b, d, f, h: ×400). Hematoxylin and eosin staining (A), papanicolaou staining (B), and immunostainings of MUC1-core (C, D), MUC2 (E, F), and MUC5AC (G, H). The tumor cells consistently expressed MUC2 and MUC5AC, but were negative for MUC1 core, histologically and cytologically.
FIGURE 4. Representative images of the pancreaticobiliary subtype IPMN. Histology (a, c, e, g: ×200); cytology (b, d, f, h: ×400). Hematoxylin and eosin staining (A), papanicolaou staining (B), and immunostainings of MUC1 core (C, D), MUC2 (E, F), and MUC5AC (G, H). The lesion was at least focally positive for MUC1 core and consistently expressed MUC5AC but not MUC2. Histologically and cytologically, immunostaining status was identical.
IPMN – Gastric Subtype may have ↑CEA

Fig. 1  Cyst fluid carcinoembryonic antigen (CEA) concentrations (log scale) according to epithelial subtypes of intraductal papillary mucinous neoplasms (n = 60). Epithelial subtype was significantly associated with cyst fluid CEA concentration (P = 0.012, Kruskal–Wallis test).

EUS-nCLE
(needle confocal laser endomicroscopy)

nCLE

Cook 19 G FNA

Mauna Kea Technologies AQ-Flex 19
Pancreatic Cysts: nCLE

ATRAUMATIC DIFFUSE SAMPLING
Pancreatic Cysts: nCLE
AGA #1204 An International, Multi-Center Trial on Needle-Based Confocal Laser Endomicroscopy (nCLE): Results From the In Vivo CLE Study in the Pancreas With Endosonography of Cystic Tumors (INSPECT)


ASGE #500 Diagnosis of Pancreatic Cysts: Endoscopic Ultrasound, Through-the-Needle Confocal Laser-Induced Endomicroscopy and Cystoscopy Trial (DETECT)

Yousuke Nakai, Takuji Iwashita, Do Hyun Park, Jason B. Samarasena, John G. Lee, Kenneth J. Chang
nCLE

- Presence of villous structures high specificity for Mucinous Neoplasia
- But sensitivity only 59%

Can we improve nCLE with “red flag” technology?

- EUS can only detect obvious nodule
- For Barrett’s, we have endoscopy & NBI
- Why not do “cystoscopy” to guide nCLE?

SpyGlass probe, Boston Scientific
DETECT Study

- 30 pts with PCNs underwent EUS-guided dual through-the-needle imaging (cystoscopy and nCLE)
- Specific features associated with clinical diagnosis of mucinous cysts identified: Mucin on cystoscopy and papillary projections, dark rings on nCLE.
- The sensitivity of cystoscopy was 90% (9/10), and that of nCLE was 80% (8/10), and the combination was 100% (10/10) in 18 "high certainty" cases.
- Conclusion: the combination of EUS-guided cystoscopy and nCLE of pancreatic cysts appears to have strong concordance with the clinical diagnosis of PCNs.

Nakai, Iwashita, Park, Samarasena, Lee, Chang GIE. 2015 (in press)
EUS-guided “through the needle” Cystoscopy

<table>
<thead>
<tr>
<th></th>
<th>SCA</th>
<th>MCN</th>
<th>IPMN</th>
</tr>
</thead>
<tbody>
<tr>
<td>Smooth wall</td>
<td>Clear fluid</td>
<td>Smooth wall</td>
<td>Papillary projections</td>
</tr>
<tr>
<td></td>
<td></td>
<td>Cloudy fluid</td>
<td>Cloudy fluid</td>
</tr>
</tbody>
</table>
Cystoscopy

SCA

MCN

IPMN

Nakai, Iwashita, Park, Samarasena, Lee, Chang GIE. 2015 (in press)
String Sign (>3mm)

Nakai, Iwashita, Park, Samarasena, Lee, Chang GIE. 2015 (in press)
A novel approach to the diagnosis of pancreatic serous cystadenoma: needle-based confocal laser endomicroscopy

Bertrand Napoléon¹, Anne-Isabelle Lemaistre², Bertrand Pujol¹, Fabrice Caillol³, Damien Lucidarme⁴, Raphaël Bourdariat⁵, Blandine Morellon-Mialhe², Fabien Fumex¹, Christine Lefort¹, Vincent Lepilliez¹, Laurent Palazzo⁶, Geneviève Monges⁷, Bernard Filoche⁴, Marc Giovannini³

CONTACT Multi-center, 31 patients
100% specificity for serous cyst adenomas

Sensitivity of nCLE : 69%
Specificity of nCLE : 100%

Napoléon B. Endoscopy 2015; 47: 26–32
EUS nCLE: Serous Cystadenoma
Conclusions

- Cyst fluid CEA does not appear to predict malignant transformation
- Clinical decision-making based on cyst size alone is inadequate
- String test & nCLE helpful for mucinous cyst
- Histologic subtyping and degree of dysplasia is important for risk-stratification (need new techniques)
- Vascular network on nCLE is very specific for Serous Cystadenoma
### High Risk Stigmata

- EUS-FNA ± nCLE

#### c/w Serous Cystadenoma

- No further work-up

#### c/w IPMN

- Worrisome features:
  - Thicken wall
  - New mural nodule
  - Rapid ↑ size
  - Family Hx CA
  - Suspicious Cytology
  - Aggressive Sub-type

#### c/w Mucinous Cystadenoma

- Surgery

#### Solitary cyst

- Distal Pancreas
- Female (+)
- String Sign (+)
- CEA (+) nCLE

- EUS ± FNA in 6 mo
- Then alternate MRCP/EUS q 1yr

### Algorithm

- Cyst > 1cm
  - Imaging
  - Non-specific

- Surgery

- Yes

- No

- Jaundice
- Enhancing Solid component
- Main PD ≥ 10mm

- No

- Surgery

- Yes
Outline

- Recognizing IPMN
- Risk stratification of IPMN
- Algorithm for Panc Cyst
- When to suspect PanIn
- Work-up for PanIn
Case: High Risk Family History

- 49 yo asymptomatic male, with family history of pancreatic cancer (father and brother)
- Ca19-9 normal
- CT of abdomen normal
Inherited susceptibility to PC

- Inheritance involved in ~10-20% of pancreatic cancers
  - Familial cancer syndromes (10%)
  - Idiopathic familial PC (80%)
  - Apparently sporadic PC (~ 10%)
**Familial Cancer Syndromes**

<table>
<thead>
<tr>
<th>Syndrome</th>
<th>Gene</th>
<th>Locus</th>
<th>PC risk until 70 yrs</th>
</tr>
</thead>
<tbody>
<tr>
<td>Peutz-Jeghers</td>
<td>LKB1</td>
<td>19p13.3</td>
<td>36%</td>
</tr>
<tr>
<td>FAMMM-PC</td>
<td>CDKN2a</td>
<td>9p21</td>
<td>17%</td>
</tr>
<tr>
<td>HBOC</td>
<td>BRCA1/2</td>
<td>13p12-13</td>
<td>3.9-8.0</td>
</tr>
<tr>
<td>HNPCC</td>
<td>MLH1, MSH2</td>
<td>2p21-22; 3p21-23; 2p16</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>FAP</td>
<td>APC</td>
<td>5p21-22</td>
<td>&lt;5%</td>
</tr>
<tr>
<td>Ataxia telangiectasia</td>
<td>ATM</td>
<td>11q22.3</td>
<td>&lt;5%</td>
</tr>
</tbody>
</table>
Familial Pancreatic Cancer

Definition: kindred with 2 or more FDR with PC
- Absence of a high incidence of other cancers or diseases known to be familial
- may also include multiple second-degree relatives with PC and/or those with young age of onset (<50 years)

Segregation analysis suggests, a yet unknown, dominant susceptibility gene carried by approximately 7 of 1,000 individuals
- Appears autosomal dominant; variable penetrance
## Risk of Pancreas Cancer

<table>
<thead>
<tr>
<th>Individual</th>
<th>Risk</th>
<th>Age 50</th>
<th>Age 70</th>
</tr>
</thead>
<tbody>
<tr>
<td>No family history</td>
<td>RR=1</td>
<td>0.05%</td>
<td>0.5%</td>
</tr>
<tr>
<td>BRCA2</td>
<td>3.5-10x</td>
<td>0.5%</td>
<td>5%</td>
</tr>
<tr>
<td>FAMMM</td>
<td>20-34x</td>
<td>1-2%</td>
<td>17%</td>
</tr>
<tr>
<td>Familial PC</td>
<td>32x</td>
<td>1.6%</td>
<td>16%</td>
</tr>
<tr>
<td>Hereditary Panc</td>
<td>50-80x</td>
<td>2.5-4%</td>
<td>40%</td>
</tr>
<tr>
<td>Peutz-Jeghers</td>
<td>132x</td>
<td>6.6%</td>
<td>36%</td>
</tr>
</tbody>
</table>

Compare: lifetime risk for CA in BE ~ 5%
Strategy

- Detect precursor lesion (dysplasia)
- Detect early cancer (< 1cm)
Normal pancreatic (duct) tissue

- PanIN-1A lesion
- PanIN-1B lesion
- PanIN-2 lesion
- PanIN-3 lesion

- IPMN
- IPMN low-grade dysplasia
- IPMN intermediate dysplasia
- IPMN high-grade dysplasia

- MCN
- MCN low-grade dysplasia
- MCN intermediate dysplasia
- MCN high-grade dysplasia

Invasive pancreatic carcinoma
Normal Pancreatic Ductal Epithelium
Pancreatic Intra-epithelial Neoplasm (PAN-IN’s)

Pan-IN-1A

Pan-IN-1B

http://pathology.jhu.edu/pancreas_panin
Pancreatic Intra-epithelial Neoplasm (PAN-IN’s)

Pan-IN-2

Pan-IN-3
Ca 19-9

- Only 50% of cancers <2cm have ↑ Ca 19-9. (Riker et al. Surg Oncol 1997)
- PPV < 1% among 71,000 asymptomatic pts. (Kim et al. J Gastroenterol Hepatol 2004)
- Lewis blood group (a-b-) are unable to synthesize Ca 19-9 (4-15% of pop.)
- Not useful (other than for baseline)
Emerging Biomarkers

- **Molecular Analysis of pancreatic juice**
  - EUROPAC study group  *Yan et al, Gastro 2005*
  - Combined K-ras, p53, and p16 mutations
  - For individuals in population of where incidence of PC is 1%, risk could be stratified between ~negligible vs >50%

- **Proteomics**
  - Biomarker discovery and development using proteomic profiling from pancreatic juice in PC, pancreatitis and normal  *Chen, Brentnall et al, Pancreas 2007*
Imaging Tests

- Multiphasic Helical CT
  - unable to detect dysplasia
  - sensitivity of detecting small lesions (<2cm) 72%
    Bronstein et al Am J Roentgenol 2004

- ERCP
  - too invasive as initial screening tool
  - eventually, may be used for PPJ analysis

- MRCP or CT/PET fusion
  - No data
Imaging Tests - EUS

- EUS is able to detect small lesions
  - Superior to Multi-detector CT (sens 98% vs 86%)  
    DeWitt et al Ann Intern Med 2004

- EUS may be able to detect dysplasia
  - 7 of 14 familial kindred found to have abnormal EUS/ERCP  
    Brentnall Ann Intern Med 1999
  - All 7 had dysplasia on surgical path
EUS: Pan-IN Correlation

R = 0.85 (p<0.007)

EUS Score

Percentage of Ducts with PanIN Lesions

EUS, CT, and ERCP

Canto et al Clin Gastroenterol Hepatol 2006

6 PJS

78 High Risk Individuals

H&P, PE, Genetic Counseling

EUS/FNA

CT

ERCP n = 65

Suspected Neoplastic lesions

No (61)

f/u EUS/CT

Yes (17)

No surgery

Surveillance (9)

Dx by FNA (1)

Surgery (7)

72 w/ 3 or more affected relatives
ALL 8 patients had pancreatic neoplasms
- Mostly branch-type IPMN’s
- Pan-IN 3

EUS - Made DX in 7 of 8

ERCP
- Made DX in 2 of 8

CT - 64 detector/3-D/MIP (max intens. proj)
- Made DX in 5 of 8;
- also found 4 extra-pancreatic neoplasms
EUS/ERCP changes

- Changes c/w chronic pancreatitis
  - EUS (78%)
  - ERCP (73%)

- Neoplastic-like lesions on EUS (17pts)
  - 1 small mass
  - 11 cystic lesions/focal dilated ducts
  - 5 nodules

- Saccular deformities on ERCP
  - (17%)

Canto et al Clin Gastroenterol Hepatol 2006
s/p Whipple: PanIn 2A
Figure 4. This figure highlights the series of steps required to allow for the early detection of curable pancreatic neoplasia. Adapted from an original illustration by Corinne Sandone, Johns Hopkins University.
Summary

- Smoking is greatest risk factor, especially in familial kindred
- High risk in hereditary pancreatitis
- Careful family history, genetic counseling is important to r/o Inherited Cancer Syndromes
- For individuals with ≥ 2 FDR, screen with EUS + CT, consider ERCP
- Biomarkers in progress
THANKS!

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