Pancreatic Neoplasms: What Can We Do?

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Pancreatic Neoplasms

• Ductal adenocarcinoma (85%)

• Neuroendocrine

• Cystic neoplasms
Pancreatic Neoplasms

- Ductal adenocarcinoma (85%)
- Neuroendocrine (6%)
- Cystic neoplasms
Objectives

• Review epidemiologic facts

• How we can identify high-risk individuals

• Early detection tools

• Multi-disciplinary treatment approach
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How Common is Pancreatic Cancer?

Compared to other cancers, pancreatic cancer is relatively rare.

<table>
<thead>
<tr>
<th>Common Types of Cancer</th>
<th>Estimated New Cases 2018</th>
<th>Estimated Deaths 2018</th>
</tr>
</thead>
<tbody>
<tr>
<td>1. Breast Cancer (Female)</td>
<td>266,120</td>
<td>40,920</td>
</tr>
<tr>
<td>2. Lung and Bronchus Cancer</td>
<td>234,030</td>
<td>154,050</td>
</tr>
<tr>
<td>3. Prostate Cancer</td>
<td>164,690</td>
<td>29,430</td>
</tr>
<tr>
<td>4. Colorectal Cancer</td>
<td>140,250</td>
<td>50,630</td>
</tr>
<tr>
<td>5. Melanoma of the Skin</td>
<td>91,270</td>
<td>9,320</td>
</tr>
<tr>
<td>6. Bladder Cancer</td>
<td>81,190</td>
<td>17,240</td>
</tr>
<tr>
<td>7. Non-Hodgkin Lymphoma</td>
<td>74,680</td>
<td>19,910</td>
</tr>
<tr>
<td>8. Kidney and Renal Pelvis Cancer</td>
<td>65,340</td>
<td>14,970</td>
</tr>
<tr>
<td>9. Uterine Cancer</td>
<td>63,230</td>
<td>11,350</td>
</tr>
<tr>
<td>10. Leukemia</td>
<td>60,300</td>
<td>24,370</td>
</tr>
<tr>
<td>11. Pancreatic Cancer</td>
<td>55,440</td>
<td>44,330</td>
</tr>
</tbody>
</table>

In 2018, it is estimated that there will be 55,440 new cases of pancreatic cancer and an estimated 44,330 people will die of this disease.

Pancreatic cancer represents 3.2% of all new cancer cases in the U.S.

3rd most common cause of death
How Common is Pancreatic Cancer?

2nd leading cause of cancer deaths by 2030

~ 60,000 deaths
How Many People Survive 5 Years Or More after Being Diagnosed with Pancreatic Cancer?

Relative survival statistics compare the survival of patients diagnosed with cancer with the survival of people in the general population who are the same age, race, and sex and who have not been diagnosed with cancer. Because survival statistics are based on large groups of people, they cannot be used to predict exactly what will happen to an individual patient. No two patients are entirely alike, and treatment and responses to treatment can vary greatly.

Based on data from SEER 18 2008-2014. Gray figures represent those who have died from pancreatic cancer. Green figures represent those who have survived 5 years or more.
How Many Survive Pancreatic Cancer?

Any improvement?

SEER 9 5-Year Relative Survival Percent from 1975-2010, All Races, Both Sexes. Modeled trend lines were calculated from the underlying rates using the Joinpoint Survival Model Software.
Pancreatic Carcinoma

• Pancreatic ductal adenocarcinoma is one of the leading causes of cancer-related mortality.

• 5 year survival for patients with PC is 8.5%

• Almost always detected in advanced stage
Pancreatic Carcinoma

What can we do?

- Prevention
  - Identify high-risk individuals
    - Screen
    - Surveillance

- Early Detection

- Expedite Treatment
The lifetime risk of developing PC in the general population is estimated to be 1.6%.

Screening not recommended for general population
FACT

**High-Risk:**

Patients having a >5% lifetime risk or 5x RR of developing PC.

Screening recommended for high-risk population

Who Gets Pancreatic Cancer?

Risk Factors

**Minor**
- Age:
  - >55
- Gender:
  - M >> F
- Race:
  - African Americans
- Cigarette smoking
- Obesity
- Diabetes

**Major**
- Chronic pancreatitis
- Pancreatic cystic lesions
- Family history of PC
- Genetic Syndromes:
  - BRCA - 2
  - Familial Melanoma
  - PRSS – 1
  - Peutz – Jeghers
  - HNPCC
Age Distribution in PC

Percent of New Cases by Age Group: Pancreatic Cancer

Pancreatic cancer is most frequently diagnosed among people aged 65-74.

Median Age At Diagnosis

70

SEER 18 2011-2015, All Races, Both Sexes
Pancreatic Cancer Risk Factors

**Smoking**

- Meta-analysis of 82 studies 2008: RR 1.7 in current and 1.2 in former smokers.

- Cigarette smoking increases the risk of pancreas cancer: 75% compared to non-smokers.

- Effect of smoking persists 10 years after cessation

Pancreatic Cancer Risk Factors

**Obesity**

- RR 2.08 with BMI >30 vs <25

- Burden study in UK: 12.8% of PC in men and 11.5% of PC in women

- Recent meta-analysis confirmed that both general obesity and abdominal obesity increases the risk of PC.


Pancreatic Cancer Risk Factors

Diabetes Mellitus

- Both type 1 and 2 doubles the risk of PC
- US National Cancer Institute study: 1.8 fold increased risk particularly in Hispanic and Asian compared to White and Blacks.
- Oral antidiabetic agents and insulin associated with reduced risk of PC

Pancreatic Cancer Risk Factors

Chronic pancreatitis

Parenchymal
- hyperechoic foci
- hyperechoic strands
- hypoechoic lobules
- cysts
- Califications
- Irregular size

Ductal
- Dilatation
- dilated SB
- irregular MD
- hyperechoic margins
- stones

Endoscopic Ultrasound

Catalano et al. Gastrointest Endosc. 2009 Jun;69(7):1251-61
Pancreatic Cancer Risk Factors

Chronic pancreatitis


RR: 2.7-5.1%
Pancreatic Cancer Risk Factors

Familial and Genetic

• Sporadic PC (85-90%)
• Genetic cause or runs in the families (10-15%)
  – Familial pancreatic cancer (FPC)
    • Pair of affected first-degree relatives (parent-child or sibling)
      – Individuals with 2 FDR: 6.4-fold risk (ie 8-12% life time risk of PC)
      – Individuals with 3 FDR: 32-fold risks (ie 40% life time risk of PC)
Pancreatic Cancer Risk Factors

Familial and Genetic

• Sporadic PC (85-90%)
• Genetic cause or runs in the families (10-15%)
  • Genetic predisposition associated with PC:
    - BRCA - 2
    - Familial Melanoma
    - PRSS – 1
    - Peutz – Jeghers
    - HNPCC
# Pancreatic Cancer Risk Factors

## Genetic

<table>
<thead>
<tr>
<th>Gene(s)</th>
<th>Common name</th>
<th>Risk of pancreatic cancer</th>
</tr>
</thead>
<tbody>
<tr>
<td>STK11/LKB1</td>
<td>Peutz-Jeghers syndrome</td>
<td>RR = 132 (95% CI, 44-261)</td>
</tr>
<tr>
<td>PRSS1</td>
<td>Hereditary pancreatitis</td>
<td>SIR = 53 (95% CI, 23-105)</td>
</tr>
<tr>
<td>CDKN2A</td>
<td>n/a</td>
<td>RR = 13-39</td>
</tr>
<tr>
<td>MLH1, MSH2, MSH6</td>
<td>Lynch syndrome*</td>
<td>RR = 9-11</td>
</tr>
<tr>
<td>TP53</td>
<td>Li-Fraumeni syndrome</td>
<td>RR = 7.3 (95% CI, 2-19)</td>
</tr>
<tr>
<td>CFTR</td>
<td>Cystic fibrosis, hereditary pancreatitis</td>
<td>RR = 5.3 (95% CI, 2.4-10.1)</td>
</tr>
<tr>
<td>APC</td>
<td>Familial adenomatous polyposis</td>
<td>RR = 4.46 (95% CI, 1.2-11.4)</td>
</tr>
<tr>
<td>BRCA2</td>
<td>n/a</td>
<td>RR = 3-9</td>
</tr>
<tr>
<td>ATM</td>
<td>Ataxia-telangiectasia</td>
<td>RR = 3.92 (95% CI, 0.44-14.2)</td>
</tr>
<tr>
<td>BRCA1</td>
<td>n/a</td>
<td>RR = 2.26 (95% CI, 1.26-4.06)</td>
</tr>
<tr>
<td>Familial pancreatic cancer in 1 or 2 first-degree relatives</td>
<td>n/a</td>
<td>RR = 4-7</td>
</tr>
</tbody>
</table>

RR: Relative risk; CI, confidence interval; SIR, standardized incidence ratio; n/a, not applicable.

*Also known as hereditary nonpolyposis colorectal cancer.
## Pancreatic Cancer Risk Factors

### Overview

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Population Exposed</th>
<th>Relative Risk</th>
<th>Attributable Fraction</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tobacco smoking</td>
<td>25-40%</td>
<td>1.5-2.2</td>
<td>PAF 11-32%</td>
</tr>
<tr>
<td><em>Helicobacter pylori</em> infection</td>
<td>25-50%</td>
<td>1.2-1.7</td>
<td>PAF 4-25%</td>
</tr>
<tr>
<td>Non-O blood group</td>
<td>50-60%</td>
<td>1.3-1.4</td>
<td>PAF 13-19%</td>
</tr>
<tr>
<td>Diabetes mellitus</td>
<td>4-17%</td>
<td>1.4-2.2</td>
<td>PAF 1-16%</td>
</tr>
<tr>
<td>Obesity</td>
<td>20-40%</td>
<td>1.2-1.5</td>
<td>PAF 3-16%</td>
</tr>
<tr>
<td>Reducing adiponectin level</td>
<td>Continuous</td>
<td>1.6*</td>
<td>PIF 11%</td>
</tr>
<tr>
<td>Increasing red or processed meat</td>
<td>Continuous</td>
<td>1.1-1.5*</td>
<td>PIF 2-9%</td>
</tr>
<tr>
<td>Heavy alcohol intake</td>
<td>Continuous</td>
<td>1.1-1.5</td>
<td>PAF &lt;9%</td>
</tr>
<tr>
<td>Family history</td>
<td>5-10%</td>
<td>1.7-1.8</td>
<td>PAF 3-7%</td>
</tr>
<tr>
<td>History of chronic pancreatitis</td>
<td>0-1%</td>
<td>2.7-5.1</td>
<td>PAF &lt;3%</td>
</tr>
<tr>
<td><em>Hepatitis B</em> infection</td>
<td>0-5%</td>
<td>1.2-1.4</td>
<td>PAF &lt;1%</td>
</tr>
<tr>
<td>History of cholecystectomy</td>
<td>4-8%</td>
<td>1.2</td>
<td>PAF &lt;1%</td>
</tr>
<tr>
<td>History of gastrectomy</td>
<td>1-2%</td>
<td>1.5</td>
<td>PAF &lt;1%</td>
</tr>
<tr>
<td>Increasing physical activity</td>
<td>Continuous</td>
<td>0.75*</td>
<td>PIF (5%)</td>
</tr>
<tr>
<td>History of allergy</td>
<td>10-20%</td>
<td>0.7-0.8</td>
<td>PPF (3-7%)</td>
</tr>
<tr>
<td>Increasing fruit or folate intake</td>
<td>Continuous</td>
<td>0.5-1.0*</td>
<td>PIF (&lt;12%)</td>
</tr>
</tbody>
</table>

* for continuous variables the relative risk is expressed for the highest versus lowest quintile
Pancreatic Cancer

Early Diagnosis
Pancreatic Carcinoma

Late Symptoms

- Jaundice
- Weight loss
- Abdominal pain
- Pruritus
- Dark urine
- Acholic stools
Pancreatic carcinoma

**Signs**

- New-onset diabetes
- Depression
Pancreatic Carcinoma

*Evaluation*

- **Blood Work**
- **Imaging**
  - US, CT, MRI/MRCP
- **Tissue sampling**
  - EUS/FNA
  - ERCP
Pancreatic Carcinoma

Blood work

- Elevated Blood Chemistries:
Pancreatic Carcinoma

Non-invasive imaging

- Abdominal US
Pancreatic Carcinoma

Non-invasive imaging

CT with oral and IV contrast:

- Normal exam
Pancreatic Carcinoma

Non-invasive imaging

- Pancreatic mass
- “double duct sign”
  - Dilated bile ducts
  - Dilated pancreatic duct

CT with oral and IV contrast:
Pancreatic Carcinoma

Non-invasive imaging

**MRI/MRCP:**
Pancreatic Carcinoma

Invasive imaging - ERCP
ERCP

Biliary and pancreatic strictures

**Goal:**

- **Sampling:**
  - biopsy, brushing
  - direct bxs (Choledochoscopy)

- **Palliation of symptom**
  - plastic vs metal stent
Sampling of Strictures

**Yield:**

- brush ~ 30%
- biopsy ~ 30%

35-50%
# Choledochoscopy

*Directed biopsies*

## Analysis of indeterminate strictures:

<table>
<thead>
<tr>
<th></th>
<th>intrinsic</th>
<th>extrinsic and intrinsic</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Sensitivity</strong></td>
<td>78% (21/27)</td>
<td>59% (23/39)</td>
</tr>
<tr>
<td><strong>Specificity</strong></td>
<td>64% (7/11)</td>
<td>75% (3/4)</td>
</tr>
<tr>
<td><strong>Positive Predictive Value</strong></td>
<td>95% (21/22)</td>
<td>100% (23/23)</td>
</tr>
<tr>
<td><strong>Negative Predictive Value</strong></td>
<td>58% (7/12)</td>
<td>20% (3/15)</td>
</tr>
</tbody>
</table>

K.F. Binmoeller et al. Results from Biopsy of Indeterminate Biliary Strictures Does Direct Visualization Help? A Multicenter Experience
Pancreatic Carcinoma

Invasive imaging - EUS

Endoscopic Ultrasound:
Endoscopic Ultrasound
Pancreatic cancer

Tissue acquisition: FNA
Endoscopic Ultrasound - FNA

**Sensitivity**

<table>
<thead>
<tr>
<th>Lesion Size (mm)</th>
<th>n</th>
<th>CT sensitivity</th>
<th>EUS FNA cytology correct</th>
</tr>
</thead>
<tbody>
<tr>
<td>≤ 10</td>
<td>16</td>
<td>6%*</td>
<td>78%</td>
</tr>
<tr>
<td>11-20</td>
<td>34</td>
<td>38%*</td>
<td>81%</td>
</tr>
<tr>
<td>21-30</td>
<td>23</td>
<td>61%*</td>
<td>91%</td>
</tr>
<tr>
<td>&gt;30</td>
<td>34</td>
<td>91%</td>
<td>95%</td>
</tr>
<tr>
<td></td>
<td>107</td>
<td>55%*</td>
<td>87%</td>
</tr>
</tbody>
</table>

*p<.005 compared with EUS sensitivity

Patel, Catalano, Geenen et al. GIE 2005
Endoscopic Retrograde Cholangiopancreatography (ERCP)

**Biliary stenting**

- Safe and effective in palliating obstructive jaundice

**CAREFUL PATIENT SELECTION**
**EMPLOY GOOD TECHNIQUE**

Plastic vs Metal
Pancreatic Carcinoma

ERCP-Palliation

• **GOAL:**
  Reestablish biliary drainage  
  symptom relief

- Jaundice
- Pruritus
- Abdominal pain
- Nausea/vomiting
Stenting Strictures

*Plastic*

- Patency: 3-5 mo
- Removable
- Inexpensive
Stentig Strictures

*Metal*

- Patency: 9-12 mo
- Expensive +/- removable
Cystic Lesions of the Pancreas

Primary Cystic Neoplasms

- Serous cystadenoma
- Pseudopapillary tumor
- Mucinous cystadenoma
- IPMN

Congenital Cysts
- Simple Cyst
- Duplication cyst

Acquired Cysts
- Pseudocyst
Cystic Neoplasms of the Pancreas
Cystic Neoplasms of the Pancreas

*Mucinous cystadenoma/carcinoma*

- Macrocystic lesions
- Viscous, mucoid fluid
- Fluid analysis: high CEA, low amylase, DNA analysis
- Mucin-secreting epithelial cells
- **Malignant potential**
Intraductal Papillary Mucinous Neoplasm (IPMN)

- First described in 1982
- Proliferation of mucus-producing ductal epithelial cells.
- Precancerous lesion
- Rate of progression to carcinoma slow

**features:**
- Patulous ampullary orifice
- Dilated pancreatic duct
- Mucus secretion
Intraductal Papillary Mucinous Neoplasm (IPMN)
Evaluation of Intraductal Papillary Mucinous Neoplasm (IPMN)

Current limitations:

Pre-operative planning:

- Whipple
- Distal pancreatectomy
- Total pancreatectomy

What is the extent of disease?
Is there multi-centric disease (~20%)?

Hidetoshi et al. Cancer 107:2567
Intraductal Papillary Mucinous Neoplasm (IPMN)

Diagnosis?

Treatment?
Pancreatic Carcinoma

Evaluation

Pt with suspected pancreatic ca

Non-invasive imaging

EUS-FNA

surgery

ERCP
Pancreatic Carcinoma

Conclusion

✓ Recognize patients @ high-risk of developing PC.
  • Familial
  • Genetic
  • Chronic pancreatitis
  • Pancreatic cystic neoplasms
  • New-onset diabetes
  • Obesity
  • Smoking
  • Age

✓ Understand the modalities available for diagnosing pancreatic cancer:
  • EUS
Pancreatic Carcinoma

Conclusion

☑ Understand the *general therapies* available:

• Surgery for those with resectable disease
• Neoadjuvant therapy for borderline patients
• Endoscopic palliation