Pancreatic Cancer
From Diagnosis to Treatment

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Objectives

• Incidence of Pancreatic cancer
• Risk factors
• Clinical Presentation
• Endoscopic Diagnosis
  – ERCP
  – EUS
• Endoscopic Management
  – Biliary Stenting
  – Pain control
  – Endoscopic-guided therapy
Pancreatic Cancer

- 43,920 diagnosed in 2012
- 37,390 pancreatic cancer deaths in 2012
- 25% 1 yr. survival
- 5% 5 yr. survival
- 20% 5 yr. survival for patients undergoing resection
2012 Estimated US Cancer Cases*

**Men** 848,170  
Prostate 29%  
Lung & bronchus 14%  
Colon & rectum 9%  
Urinary bladder 7%  
Melanoma of skin 5%  
Kidney & renal pelvis 5%  
Non-Hodgkin lymphoma 4%  
Oral cavity 3%  
Leukemia 3%  
Pancreas 3%  
All Other Sites 18%

**Women** 790,740  
Breast 29%  
Lung & bronchus 14%  
Colon & rectum 9%  
Uterine corpus 6%  
Thyroid 5%  
Melanoma of skin 4%  
Non-Hodgkin lymphoma 4%  
Kidney & renal pelvis 3%  
Ovary 3%  
Pancreas 3%  
All Other Sites 20%  

*Source: American Cancer Society, 2012*

*Excludes basal and squamous cell skin cancers and in situ carcinomas except urinary bladder.*
2012 Estimated US Cancer Deaths

<table>
<thead>
<tr>
<th>Cancer Site</th>
<th>Men 301,820</th>
<th>Women 275,370</th>
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<tbody>
<tr>
<td>Lung &amp; bronchus</td>
<td>29%</td>
<td>26%</td>
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<tr>
<td>Prostate</td>
<td>9%</td>
<td>14%</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>9%</td>
<td>9%</td>
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<tr>
<td>Pancreas</td>
<td>6%</td>
<td>7%</td>
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<tr>
<td>Liver &amp; intrahepatic bile duct</td>
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<tr>
<td>Leukemia</td>
<td>4%</td>
<td>4%</td>
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<tr>
<td>Esophagus</td>
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<tr>
<td>Urinary bladder</td>
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<td>3%</td>
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<tr>
<td>Non-Hodgkin lymphoma</td>
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<td>2%</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>3%</td>
<td>2%</td>
</tr>
<tr>
<td>All other sites</td>
<td>25%</td>
<td>24%</td>
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Cancers that are in red are among the top 10 causes of cancer death in the US that year.
Trends in Five-year Relative Survival (%)*, 1975-2007

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<thead>
<tr>
<th></th>
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<tr>
<td>All sites</td>
<td>49</td>
<td>56</td>
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<tr>
<td>Breast (female)</td>
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<td>Rectum</td>
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<td>Urinary bladder</td>
<td>73</td>
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*5-year relative survival rates based on follow up of patients through 2008.
Source: Surveillance, Epidemiology, and End Results Program, 1975-2008, Division of Cancer Control and Population Sciences, National Cancer Institute, 2011.
Pancreatic Cancer

- Risk factors
  - Smoking
  - Diabetes
  - Chronic Pancreatitis
  - African American
  - Hereditary pancreatic cancer syndromes
  - Familial pancreatic cancer (FPC)
Pancreatic Cancer Distribution

- Sporadic (~85%)
- Known Genetic Syndromes (~5%)
- Familial Pancreatic Cancer (~10%)

Hereditary Pancreatic Cancer Syndromes

1. BRCA2 and Pancreatic Cancer
   - Present in **17-19%** of patients with at least 2 or more affected individuals
   - Present in **5-10%** of patients with pancreatic cancer without family history
   - **1%-2%** Ashkenazi Jews

2. Peutz-Jeghers syndrome (STK11/LKB1)
   - 36% cumulative risk age 15-64

3. FAMMM p16(CDKN2A)
   - Autosomal Dominant
   - Lifetime risk **16%**
Familial Pancreatic Cancer (FPC)

- **Definition**: At least 2 FDR affected without accumulation of other cancers or familial diseases
  - **18-fold** increase in relatives with 2 First-Degree Relatives (FDR) affected
  - **57-fold** increase in relatives with 3 family members affected
  - *BRCA2 (17-19%)*
## Risk of Pancreatic Cancer
**Genetic syndromes**

<table>
<thead>
<tr>
<th>Individuals</th>
<th>Risk</th>
<th>Age 50</th>
<th>Age 70</th>
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<td><strong>No History</strong></td>
<td>1</td>
<td>0.05%</td>
<td>0.5%</td>
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<tr>
<td><strong>BRCA 2</strong> (Breast-Ovarian)</td>
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<td><strong>P16</strong> (FAMMM)</td>
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<tr>
<td><strong>Familial</strong></td>
<td>14-32</td>
<td>0.8-1.6%</td>
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<tr>
<td><strong>STK11/LKB1</strong> (Peutz-Jeghers)</td>
<td>132</td>
<td>6.6%</td>
<td>30-60%</td>
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Clinical Presentation

- Painless jaundice
- Dark urine, light stool
- Pancreatitis
- Abdominal pain/back pain
- Weight loss
- Loss of appetite
Diagnosis

- **Radiology Studies**
  - Abdominal Ultrasound
  - CAT scan
  - MRI/MRCP
  - PET scan

- **Gastroenterology Procedures**
  - ERCP
  - Endoscopic Ultrasound

- **Blood tests**
  - Liver enzymes and amylase/lipase
  - Tumor Markers- CA 19-9
ERCP vs. EUS for diagnosis
Diagnostic ERCP in pancreatic cancer

- Obtain tissue for Diagnosis
  - Cytology brushings
  - Endoscopic biopsies
## Brush Cytology in Malignant Biliary Strictures

<table>
<thead>
<tr>
<th>Authors</th>
<th>YR</th>
<th>PT’s</th>
<th>Ca.</th>
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<th>Se</th>
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<td>39%</td>
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<td>96%</td>
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<td><strong>Total</strong></td>
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*De bellis et al, GIE 2002*
# ERCP-guided Biopsy of Malignant Biliary Strictures

<table>
<thead>
<tr>
<th>Authors</th>
<th>YR</th>
<th>PT’s</th>
<th>Ca.</th>
<th>TP</th>
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<th>Spe</th>
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<td>94%</td>
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<tr>
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<td>97%</td>
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</table>

*De bellis et al, GIE 2002*
## Combined Brush and Biopsy of Malignant Biliary strictures

<table>
<thead>
<tr>
<th>Authors</th>
<th>YR</th>
<th>Brush</th>
<th>Biopsy</th>
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<td>47%</td>
<td>65%</td>
<td>70%</td>
</tr>
</tbody>
</table>

*De bellis et al, GIE 2002*
EUS in Pancreatic Cancer

• EUS has become an integral part of the work-up of suspected pancreatic cancer
  – Tissue acquisition (FNA)
  – Staging to determine resectability
EUS-guided FNA in Pancreatic Cancer

• **Indications**
  – Document malignancy in patients unresectable who will be undergoing Chemotherapy/XRT
  – To exclude less common types of pancreatic cancers that may alter management
  – Patient request for a definite diagnosis prior to undergoing surgery
EUS-guided FNA in Pancreatic Cancer

- EUS-guided FNA of pancreatic masses
  - Sensitivity 85-90%
  - Specificity 97-100%
  - Accuracy 84-92%
- False negative rate of ERCP and CT-guided biopsies 20-30%
EUS Staging of Pancreatic Cancer

- **Accuracy of TNM staging**
  - T stage 74-94%
  - N stage 64-92%
  - M stage (occult liver metastasis)

- **EUS vs. Helical CT scan**
  - Sensitivity for detecting tumors 97% vs. 73%
  - Detects small tumors<2cm which are often not seen on CT scan
  - Predicting vascular invasion
EUS-guided FNA

• Safety
  – Outpatient procedure
  – EUS alone has similar risk profile to standard endoscopy
  – EUS-guided FNA adds 1% risk of pancreatitis
  – Almost no risk of tumor seeding (2 cases worldwide reported)
FNA Video
Indications

- Therapeutic Drainage of the bile duct when the patient is jaundiced and…..
  - In-operable and is planning Chemotherapy
  - Suspected cholangitis
  - Itching that is medically refractory
  - Long delay for surgery
    - *NEJM 2010* - Surgery within 1 week vs. biliary decompression for 4-6 weeks
    - Conclusion - routine pre-operative biliary drainage increases complication rate
ERCP Complications

- **Immediate**
  - Cholangitis
  - Pancreatitis
  - Bleeding
  - Perforation

- **Late**
  - Stent Occlusion
Plastic Stents

- Median Patency 3-5mos
- Average diameter is 10Fr (3.3mm)
- Stent change q3mos.

Metal Stents

- Median Patency 6-8mos
- Self expandable up to 30Fr (10mm)
- Permanent
Covered Metal Stents?

- **Removable**
  - Patency appears longer than uncovered metal stent
    - Mukai et al DDW Abstract 2012
      - 120 pts. randomized to covered vs. uncovered in patients with unresectable pancreatic cancer
      - Stent patency for covered vs. uncovered 583 vs. 314 days (p=.0194)
      - Re-intervention rate 14/60 for covered vs. 22/60 uncovered stents (23 vs. 37%)
      - Showed a patency rate of 97% at 12months in 44 pts unresectable and easily removed in the 40 patients who underwent a Whipple procedure
EUS-guided Therapy

• EUS-guided Pain management
  – Celiac plexus neurolysis
  – Celiac ganglion neurolysis
  – Celiac ganglion irradiation

• EUS-guided Fiducial marker placement
  – Used to guide radiotherapy
Fiducial Video
EUS-guided CPN

• Originally performed in 1996*
  – 30 patients with inoperable cancer
  – 88% improvement in pain score at 12 weeks
  – No complications
  – Demonstrated feasibility

*Wiersema MJ Wiersema LM, GIE 1996
EUS-guided CGN

• Levy et al. Am J Gastroenterol 2008
  – 16 cancer pts. underwent direct ganglia injections with bupivicaine/alcohol
    • 16/17 reported pain relief
    • Increase pain exacerbation after procedure correlated with improved therapeutic response
EUS-guided Irradiation

• Wang et al. GIE 2012
  – 23 pts. With unresectable pancreatic cancer underwent EUS-guided direct celiac ganglion irradiation with (125) I seeds
  – 6 patients had pain exacerbation post procedures
  – 2 weeks post procedure VAS and mean analgesic consumption significantly less than pre-op values
EUS-guided Fiducial placement

- Used in patients undergoing neo-adjuvant chemo radiation for pancreatic cancer
- Guides Stereotactic Body Radiation Therapy (SBRT)
- (INSERT VIDEO)
Summary

• Pancreatic Cancer is still a deadly disease
• EUS is best method to obtain tissue diagnosis (perform before ERCP if available)
• Trend towards using covered metal stents for biliary decompression all patients irrespective of stage
• EUS-guided interventions continue to expand
Acknowledgements

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• Prasad Kulkarni, MD
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  – Mo Malafa, MD
  – Gregory Springett, MD PhD
  – Sarah Hoffe, MD

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  – Fax 813-745-7229