Pancreatic Cancer: The Surgical Oncologist’s Perspective

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Presentation

- Symptoms
  - Unexplained weight loss
  - Vague abdominal/back pain
  - Early satiety, nausea, vomiting
  - Steatorrhea
  - Jaundice

Pancreatic Cancer

- Surgical resection is only hope for cure
  ✓ Very few present with resectable disease
- Novel approaches needed
- Early detection is a must
  ✓ High index of suspicion

Presentation

- Signs
  ✓ Elevated LFT’s
  ✓ Elevated blood glucose
  ✓ Unexplained pancreatitis
  ✓ Palpable mass
Diagnostic Work-up

- Spiral CT scan
- Surgical Consultation
- CA19-9
- ERCP
- EUS
- Biopsy
Resectability

- Resectable:
  - No metastatic disease
  - Clear fat plane around celiac axis and SMA
  - Patent SMV and portal vein
Resectability

- **Resectable:**
  - No metastatic disease
  - Clear fat plane around celiac axis and SMA
  - Patent SMV and portal vein
- **Unresectable**
  - Celiac/SMA encasement
  - Portal vein/SMV occlusion
  - Aorta/IVC invasion
Resectability

- Borderline resectable
  - Portal vein impingement
  - Tumor abutting SMA
  - Gastroduodenal artery encasement at origin
  - Limited IVC invasion
  - Short segment SMV occlusion
Treatment

- Multidisciplinary discussion
- Surgical consultation
- Preoperative biliary decompression
  - If planning neoadjuvant therapy on protocol
  - If severe symptoms or cholangitis
  - Logistics
### Biliary Decompression
- Not mandatory
- Causes inflammation in porta hepatis
- Can be endoscopic (preferred) or transhepatic
- May increase postoperative complications

### Surgical Resection
- Pancreaticoduodenectomy (Whipple)
  - Head/uncinate lesions
- Subtotal pancreatectomy
  - Neck/body lesions
- Distal pancreatectomy
  - Tail lesions

### Surgical “Controversies”
- Pylorus preservation
- Spleen preservation
- Portal vein resection
- Laparoscopy
- Prophylactic gastrojejunostomy
- Extended lymph node dissection
- Pancreas reconstruction
- Total pancreatectomy

### Pylorus Preserving Whipple
- **Pros**
  - Less ulcerogenic
  - Less dumping syndrome
- **Cons**
  - Increased delayed gastric emptying
- No difference in outcomes → surgeon choice
### Spleen Preservation

**Pros**
- Fewer complications

**Cons**
- Time consuming
- Less oncologic operation
- No real difference → surgeon preference

### Total Pancreatectomy

**Pros**
- No pancreatic anastomosis
- Complete extirpation of neck tumors

**Cons**
- Guaranteed exocrine insufficiency
- Difficult glucose control

### Laparoscopy

**For Staging**
- Detection of occult metastases
- Avoid laparotomy in up to 1/3 of patients
- Adds time, cost, and frustration
- Not good for determination of local tumor extent

**For Resection**
- Less morbid for distal/subtotal pancreatectomies
- Unproven for Whipple/total pancreatectomy

### Prophylactic Duodenal Bypass

**Pros**
- Safe operation
- Avoids future gastric outlet obstruction in unresectable patients

**Cons**
- Often doesn’t work well
- Ulcerogenic
- More recuperation
<table>
<thead>
<tr>
<th><strong>Portal Vein Resection</strong></th>
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<tbody>
<tr>
<td><strong>Pros</strong></td>
</tr>
<tr>
<td>✓ Can be done safely</td>
</tr>
<tr>
<td>✓ Extends resectability</td>
</tr>
<tr>
<td><strong>Cons</strong></td>
</tr>
<tr>
<td>✓ Risk of postoperative thrombosis</td>
</tr>
<tr>
<td>✓ Survival benefit unclear</td>
</tr>
<tr>
<td><strong>Should be done in high volume centers in multidisciplinary setting</strong></td>
</tr>
</tbody>
</table>
Surgical Complications

- Occur in 30 – 40%
- Rarely life-threatening
  - Mortality <5%
- Delayed gastric emptying (most common)
- Pancreatic fistula (most dangerous)

Long-Term Sequelae

- Diabetes
  - rare
- Pancreatic exocrine insufficiency
  - Common and easily treatable
- Marginal ulcers
  - Lifelong acid suppression
**Long-Term Sequelae**

- Post-gastrectomy syndromes
  - Dumping syndrome
  - Diarrhea
- Vitamin B12 deficiency
- Biliary stenosis (rare)

**Palliation**

- Jaundice
  - Biliary stenting
  - Biliary bypass
- Gastric outlet obstruction
  - Duodenal bypass
  - Duodenal stenting
- Pain
  - Neurolysis
Pancreatic Cancer Treatment

- Resectable → resection and CLINICAL TRIAL
- Borderline resectable → neoadjuvant on CLINICAL TRIAL and resection
- Locally advanced → CLINICAL TRIAL
- Metastatic → CLINICAL TRIAL
- When in doubt → CLINICAL TRIAL

Pancreatic Cancer

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### Pancreatic Cancer

- 4th leading cause of cancer death in US
- ~ 33,000-34,000 cases annually
- ~ 32,000 deaths annually
- Highest incidence-death ratio
- 5 year survival <5%
- Peak incidence in 7th decade of life

### Pancreatic Cancer Risk Factors

- Smoking (aromatic amines)- 2-fold increase
- Hereditary pancreatitis- risk by age 70 is 40%
- Chronic pancreatitis- 4% at 20 years of disease
- Family history-
  - 1 family member: 13-fold risk
  - 2 family members: 18-fold risk
  - 3 family members: 57-fold risk

### Pancreatic Cancer Signs & Symptoms

- Abdominal pain- up to 80%
- Painless jaundice- 50%
- Fatigue
- Weight loss
- Back pain- may represent nerve involvement (celiac plexus) and preclude surgical resection
- Steatorrhea uncommon presentation

### Pancreatic Cancer

- >90% are ductal adenocarcinomas
- Remaining cases include cystic neoplasms, neuroendocrine tumors
- 10-15% of patients are candidates for surgical resection at time of diagnosis (stage I and II)
- 50% of patients are unresectable at diagnosis (stage III and IV)
### Pancreatic Cancer Tumor Markers

- All markers lack sensitivity and specificity
- CA19-9: most sensitive ~ 70%, specificity 87%
- CA19-9 less sensitive in setting of biliary obstruction
- Other markers not as useful as they lack sensitivity and specificity or are too costly for clinical practice

### Pancreatic Cancer - EUS

- Obtain tissue with fine needle aspiration (FNA)
- Determine resectability for borderline tumors on CT
- Most accurate for local extent (T stage)
- Most accurate for lymph node involvement (N stage)
- Palliation of cancer pain with celiac plexus neurolysis

### Pancreatic Cancer Diagnosis & Staging

- CT imaging prompted by symptoms
- ERCP: “double duct” sign representing obstruction of pancreatic and bile ducts
- ERCP bile duct brushings are notoriously insensitive for malignancy
- MRCP: highly sensitive for pancreatic cancer, but is expensive

### Pancreatic Cancer Staging

- T1- tumor confined to pancreas <2cm size
- T2- tumor confined to pancreas >2cm size
- T3- tumor extends to surrounding structures such as PV, SMV, CBD, duodenum
- T4- tumor extends into stomach, spleen, colon or vascular structures SMA and celiac trunk
- N0/N1- absence/presence of LN involvement
- M0/M1- absence/presence of metastasis
Pancreatic Cancer Chemotherapy

- Fluorouracil and gemcitabine based regimens
- Limited survival benefit
- Radiation:
  - Adjuvant after resection for cure
  - Treatment of unresectable disease in combination with chemotherapy

Pancreatic Cancer Surgical Approach

- Dr. Bloomston

T1 Lesion

T3 Lesion
## T4 Lesion

### Pancreatic Cancer

#### Endoscopic Management of Complications

### Complications

- Common bile duct obstruction
- Duodenal obstruction
- Intractable pain
- Pancreatic duct obstruction (uncommon)
**Bile Duct Obstruction**

- CBD obstruction can lead to vitamin K deficiency
- Cholangitis rare in malignant biliary obstruction
- Cholangitis can complicate endoscopic biliary drainage procedures
- Goals of therapy:
  - Relieve jaundice and pruritis
  - Biliary drainage in preparation for chemotherapy
  - Biliary drainage for surgery prep and palliation

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**Bile Duct Obstruction-Stents**

- Self Expanding Metal Stents (SEMS):
  - Longer patency: 6 to 9 months
  - Technically more difficult deployment
  - Permanent and not removable
  - Interferes with radiation treatment & surgical field
  - Palliation for patients: life expectancy >6 months
  - No effect on patient survival
  - Less tumor in-growth/obstruction with covered vs. uncovered SEMS

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**Bile Duct Obstruction-Stents**

- Different stents, different indications
- Plastic Stents:
  - Technically easy deployment
  - Patency: 2 to 3 months, needs changing
  - No interference with external beam radiation
  - Removable but can migrate proximal or distal
  - Will not interfere with surgical field
  - Bridge to definitive therapy (surgery)
  - No effect on survival

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**Complications- Bowel Obstruction**

- Direct compression of duodenum by mass
- Surrounding inflammatory reaction with edema contributes to luminal narrowing
- Reduced duodenal motility
- Symptoms of gastric outlet obstruction or small bowel obstruction
- Goal of therapy:
  - Reduce symptoms
  - Improve oral intake and nutrition
  - Pleasure of eating
Complications-Bowel Obstruction

- Complications of stent placement are essentially that of EGD
- Diet limitations after placement- low residual liquid to soft mechanical diet
- Increase in bowel perforation when balloon dilation is required to place SEMS
Symptom relief in 80-90% in 2-3 days

Re-intervention required in 20-25%:
  ✓ Stent occlusion, migration and bowel perforation

Complications-Bowel Obstruction

Cystic Lesions of the Pancreas

Intractable Pain

- Due to involvement of celiac neural plexus, located on either side of celiac arterial trunk
- Initial symptom of pain at diagnosis confers poor prognosis
- Pain leads to poor PO intake, weight loss and poor quality of life
- Goals of therapy:
  ✓ Decrease pain, improve PO intake and weight, improve quality of life and functional status

Cystic Lesions of Pancreas

- Widespread use of imaging (CT) has led to increased detection of cystic lesions of the pancreas
- Incidentally discovered mostly, some discovered due to jaundice, pain, or pancreatitis
- Often confused or misdiagnosed as pseudocysts based on clinical history
<table>
<thead>
<tr>
<th>Types of Pancreatic Cysts</th>
<th>Serous Cystic Neoplasm- SCN</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Benign, pre-malignant and malignant</td>
<td>• Nearly universally benign lesion</td>
</tr>
<tr>
<td>• Most are pseudocysts- 90%</td>
<td>• Approximately 25% of cystic lesions</td>
</tr>
<tr>
<td>• Cystic neoplasms- 10%</td>
<td>• Often patients have surgical resection for benign entity</td>
</tr>
<tr>
<td>✓ Serous cystic neoplasms</td>
<td>• Advancements in pancreatic imaging aim to reduce this occurrence</td>
</tr>
<tr>
<td>✓ Mucinous cystic neoplasms</td>
<td></td>
</tr>
<tr>
<td>✓ Mucinous cystadenocarcinomas</td>
<td></td>
</tr>
<tr>
<td>✓ Intraductal Papillary Mucinous Neoplasms main duct and side-branch varieties</td>
<td></td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Cystic Lesions Prevalence</th>
<th>SCN Image Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td>• Some autopsy studies- 73/300 (24%)</td>
<td>• CT: Microcystic, often with central stellate scar</td>
</tr>
<tr>
<td>• In U.S.- nearly 20%</td>
<td>• Difficult to determine communication with pancreatic duct (differentiate with IPMN)</td>
</tr>
<tr>
<td>• Increases with age</td>
<td>• EUS: Microcystic with central stellate scar</td>
</tr>
<tr>
<td>• Located throughout the pancreas</td>
<td>• Much easier to document pancreatic duct communication</td>
</tr>
<tr>
<td>• Cyst epithelium: benign epithelium, atypical hyperplasia and carcinoma in situ</td>
<td></td>
</tr>
</tbody>
</table>
### Mucinous Cystic Neoplasm - MCN

- Pre-malignant or malignant lesions
- Discrete individual cysts/compartments
- Difficult to distinguish between MCN and IPMN lesions radiographically
- Difficult to distinguish between MCN and macrocystic SCN
- Demographic overlap with SCN and IPMN

<table>
<thead>
<tr>
<th>MCN Image Characteristics</th>
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<tr>
<td><strong>CT:</strong></td>
</tr>
<tr>
<td>✓ Macrocystic, unilocular with occasional septations</td>
</tr>
<tr>
<td>✓ Difficult to image mural nodularity and communication with main pancreatic duct</td>
</tr>
<tr>
<td><strong>EUS:</strong></td>
</tr>
<tr>
<td>✓ Macrocystic unilocular with occasional septations</td>
</tr>
<tr>
<td>✓ Better assessment of mural nodularity and communication with main pancreatic duct</td>
</tr>
</tbody>
</table>

### Intraductal Papillary Mucinous Neoplasm - IPMN

- Main duct and side-branch varieties
- Strong tendency for malignant transformation
- Difficult to distinguish between MCN and side-branch IPMN
- Side-Branch type can be single focus or multifocal

<table>
<thead>
<tr>
<th>IPMN Image Characteristics</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Side-Branch type:</strong></td>
</tr>
<tr>
<td>✓ CT/MRI/MRCP: Unilocular without septations, +/- communication with main pancreatic duct</td>
</tr>
<tr>
<td>✓ EUS: Unilocular +/- septations and communication with main pancreatic duct</td>
</tr>
<tr>
<td><strong>Main duct type:</strong></td>
</tr>
<tr>
<td>✓ CT/MRI/MRCP: Main pancreatic duct dilation, difficult to image mural nodularity or solid component</td>
</tr>
<tr>
<td>✓ EUS: Main pancreatic duct dilation, mural nodularity and solid component more readily visualized</td>
</tr>
</tbody>
</table>
**Clinical Presentation**

- Most cysts are asymptomatic
- Incidentally discovered with imaging performed for other reasons
- Symptoms usually due to pancreatitis but can uncommonly present as jaundice
- Can be confusing as cystic lesions can be mistaken for pseudocysts

**Pancreatic Cyst Demographics**

<table>
<thead>
<tr>
<th>Cyst/Tumor</th>
<th>Sex</th>
<th>Age</th>
<th>Appearance</th>
<th>Histology</th>
<th>Risk of Malignancy</th>
</tr>
</thead>
<tbody>
<tr>
<td>Serous Cystic Neoplasm</td>
<td>F</td>
<td>Middle age</td>
<td>Microcystic</td>
<td>Carcinogenic</td>
<td>Low</td>
</tr>
<tr>
<td>Mucinous Cystic Neoplasm</td>
<td>F</td>
<td>Middle age</td>
<td>Macrocystic/microcystic</td>
<td>Mucinous, columnar epith., ovarian stroma</td>
<td>Moderate</td>
</tr>
<tr>
<td>Mucinous Cystic Adenocarcinoma</td>
<td>F</td>
<td>Middle Age</td>
<td>Associated mass, mural nodularity</td>
<td>Mucinous, malignant</td>
<td>High</td>
</tr>
<tr>
<td>IPMN</td>
<td>M/F</td>
<td>Elderly</td>
<td>Unilocular</td>
<td>Papillary, mucinous</td>
<td>Moderate-High</td>
</tr>
<tr>
<td>Cystic Endocrine Tumor</td>
<td>M/F</td>
<td>Middle Age</td>
<td>Associated mass</td>
<td>Endocrine</td>
<td>Low</td>
</tr>
<tr>
<td>Pseudopapillary Tumor</td>
<td>F</td>
<td>Young</td>
<td>Associated mass</td>
<td>Mixed solid and cystic-endocrine</td>
<td>Low</td>
</tr>
</tbody>
</table>

**Differential Diagnosis**

- Most important: distinguish mucinous cystic neoplasms and IPMN from serous cystic lesions (benign from potentially malignant)
- Ramifications for further management such as surgery vs. surveillance

**Diagnostic Methods**

- RUQ ultrasound not helpful- poor pancreatic visualization
- MRCP can demonstrate ductal dilation and communication with cyst
- CT:
  - Mode most often responsible for finding lesion
  - Unilocular or macrocystic features
  - Main pancreatic duct dilation in IPMN
  - Communication with main PD in side-branch type
## Diagnostic Methods

- CT/MRI in general not sufficient to determine lesion type or presence of malignancy
- EUS:
  - Very sensitive for cyst type
  - FNA further differentiates lesion type
  - FNA safety profile very good

### Serous Cystic Neoplasm

[Images of CT/MRI scans of serous cystic neoplasm]
<table>
<thead>
<tr>
<th>Mucinous Cystic Neoplasm</th>
<th>Side-Branch Intraductal Papillary Mucinous Neoplasm</th>
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</thead>
<tbody>
<tr>
<td>MCN with Mural Nodule</td>
<td>Main Duct Intraductal Papillary Mucinous Neoplasm</td>
</tr>
</tbody>
</table>
Diagnosis

Cyst FNA

- Mucin in aspirated fluid is moderately predictive of mucinous neoplasm
- CEA, CA 72-4, CA 19-9, amylase, lipase and fluid viscosity can be used
- CEA, amylase and "string test" for mucin are most commonly used and most accurate

Prediction of pancreatic cystic neoplasm by using results of cyst fluid analysis formula (SCN vs MCN)

<table>
<thead>
<tr>
<th>Cyst</th>
<th>Cyst fluid analysis formula</th>
<th>Sensitivity</th>
<th>Specificity</th>
<th>+</th>
<th>-</th>
<th>Accuracy</th>
</tr>
</thead>
<tbody>
<tr>
<td>PC</td>
<td>VIS &lt;1.6 or lipase UL &gt;6000 and CEA ng/mL &lt;480</td>
<td>91.3</td>
<td>100</td>
<td>100</td>
<td>86.0</td>
<td>97.2</td>
</tr>
<tr>
<td>SCN</td>
<td>VIS &lt;1.6 and lipase UL&gt;8000</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
<td>100</td>
</tr>
<tr>
<td>MCN</td>
<td>VIS ≥1.6 and CEA ng/mL &lt;6000</td>
<td>85.7</td>
<td>100</td>
<td>100</td>
<td>96.2</td>
<td>97.2</td>
</tr>
<tr>
<td>MCN-CA</td>
<td>VIS ≥1.6 and CEA ng/mL ≥8000</td>
<td>100</td>
<td>92</td>
<td>84.0</td>
<td>100</td>
<td>94.3</td>
</tr>
</tbody>
</table>

Results of cyst fluid analysis SCN vs MCN: EUS-FNA

<table>
<thead>
<tr>
<th>Parameters</th>
<th>Benign/inflammatory</th>
<th>Premalignant/malignant</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>PC (n = 23)</td>
<td>SCN (n = 13)</td>
</tr>
<tr>
<td>VIS</td>
<td>1.3 (1.5-1.5-1.3)</td>
<td>1.2 (1.5-1.6)</td>
</tr>
<tr>
<td>Amylase (UL)</td>
<td>2216 (2000-10,140)</td>
<td>680 (50-1700)</td>
</tr>
<tr>
<td>Lipase (UL)</td>
<td>10,660 (8150-12,000)</td>
<td>540 (50-2000)</td>
</tr>
<tr>
<td>CEA (ng/mL)</td>
<td>194 (30-432)</td>
<td>121 (20-310)</td>
</tr>
<tr>
<td>CA 19-9 (U/L)</td>
<td>50,400 (225-100,000)</td>
<td>490 (230-700)</td>
</tr>
</tbody>
</table>

P < .001 MCN and MCN-CA vs PC and SCN.
1 P < .001 PC vs all others.
2 P < .001 PC vs all others.
3 P < .001 MCN-CA vs all others.
4 P < .001 SCN vs MCN-CA.

So What Do We Do About It?
### SCN and MCN Lesions

- Decision tree based on a few things:
  - Life expectancy
  - Cyst size
  - Cyst appearance
  - Pseudocyst?
  - Symptoms
  - Surgical risk

### IPMN

- Cyst size, appearance, location important
- Head (Whipple) vs body/tail (sub-total pancreatectomy)
- Side-Branch:
  - Size greater than 3cm - resect
  - Mural nodularity, solid component - resect
- Main duct:
  - Resect all if possible
  - Full duct length involvement is problematic

### IPMN

- Worst prognosis:
  - Adenocarcinoma from mucinous lesions
  - 20-30% survival at 5 years (generous)
- Side-branch variety:
  - Malignant transformation: 15-20% at 5 yr
- Main duct:
  - Malignant transformation: 45-50% at 5 yr

### Prognosis

- Cystic lesions are slow growing
- Appropriate imaging and surveillance reduces likelihood of malignancy