Surgery for Pancreatic Cancer

Charles M. Vollmer Jr., MD, FACS
Associate Professor of Surgery
Director of Pancreatic Surgery

Penn 200 Medical Students
Today’s Journey

Purpose: To get you in my head

- Scope of the problem
- Diagnosis, Staging, Treatment
- Endoscopy, Radiology
- Surgical Approaches
- Expected Outcomes and Recovery
- Adjunct Care
Case Scenario

A 65 year old retired executive presents with jaundice, epigastric pain, mid-back pain and weight loss. Physical exam demonstrates obvious jaundice and a globular mass in the right upper quadrant.
Case Scenario

A 65 year old retired executive presents with jaundice, epigastric pain, mid-back pain and weight loss. Physical exam demonstrates obvious jaundice and a globular mass in the right upper quadrant.

It's that simple.... and this complex...
Pancreatic Cancer

USA Updated 2012 Statistics

- 43,000 estimated new cases
- 40,000 estimated deaths
- 5-year survival 4%
- 4th leading cause of cancer deaths
The Five Most Common Solid Tumors 2006

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Presentation

Nonspecific: anorexia, weight loss, weakness, pruritis

Invasive or obstructive symptoms:
- Jaundice
- Pain
- Gastric outlet obstruction

Less common:
- Glucose intolerance
- Acute pancreatitis
- Trousseau’s syndrome

Distal Cancers (10%)
- Weight Loss, Back Pain, Anorexia, Diarrhea
What’s first for our patient?
Painless Obstructive Jaundice
Endoprosthesis Biliary Stents

Which patients should be stented?

Infectious complications

What stent?

Typically obeys referral patterns and flow

Keep this at or below Cystic Duct take-off
Our job is to ask two questions...
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Can we do it?
Staging

Assessment of resectability by CT-Angiography (M,N,T)

- Absence of metastasis
- *Distant* Lymph Node Involvement
- No encasement or obstruction of celiac, hepatic, proximal GDA or SMA
- No narrowing or occlusion of SMV, distal Splenic, or Portal veins
CT Cholangio-Pancreatogram

Double-Duct Sign
CT Portography

"Tumor appears resectable by CT Criteria"
Pre-Operative Determination of Regional Vascular Anatomy

Safety & Staging

- Celiac Axis
- Superior Mesenteric Artery
- GDA
- LHA
- R-RHA
Three Classes of Tumors

Clearly Resectable

Aaaah!
Three Classes of Tumors

Clearly Unresectable

UGGH!
Three Classes of Tumors

Borderline Resectable

Hmmmh???
What is Borderline Unresectability?
Raptopolous Grade 0

No involvement of critical vasculature (PV, SMV, SMA/Celiac)
Fat plane or normal pancreas between tumor and vessel
Raptopolous Grade 1

Loss of fat plane between tumor and vessel with, or without, smooth displacement of vessel
Raptopolous Grade 2

Flattening or slight irregularity of one side of the vessel
Raptopolous Grade 3

Tumor extending around at least 2/3 vessel perimeter, altering its contour and narrowing the lumen
Raptopolous Grade 4

Occluded / obliterated vessel

PV

TUMOR

P

GE

SMV
Two Tools For This

Vascular Resections
- Veins - Yes
- Arteries - Rarely

Neoadjuvant Therapy

*Promise*…*not yet fulfilled.*
Unresectable Pancreatic Cancer

• Dual-Contrast thin-cut Abdominal CT Scan
• Tissue Diagnosis (EUS)
• ERCP with Stent
• Avoid Surgery whenever possible
• Medical Oncology referral
• Palliative Care
  ➢ Chemotherapy
  ➢ Radiation therapy if not metastatic
    ➢ Cyberknife/Protons
So, what if it’s a go?
Preoperative Biopsy

- CT or US guided FNA can be obtained safely with sensitivity of 50-70%, false negative rate of ~ 10%
- Theoretically could cause shedding of tumor cells
- Histologic diagnosis is not required for the majority of patients who are candidates for resection
- Should be reserved for establishing diagnosis in patients who are not resectable and those undergoing neoadjuvant protocols for locally advanced disease
HPB Malignancy

Problem

Operability ≠ Resectability
Staging Laparoscopy with Ultrasonography

Conclusion: Patients can be spared useless laparotomy
Laparoscopic Ultrasound

Consider a dedicated radiologist as part of the “Team”
Utility of Staging Laparoscopy in Subsets of Peripancreatic and Biliary Malignancies

Charles M. Vollmer, MD,* Jeffrey A. Drebin, MD, PhD,* William D. Middleton, MD,† Sharlene A. Teefey, MD,† David C. Linehan, MD,* Nathaniel J. Soper, MD,* Christopher J. Eagon, MD, and * Steven M. Strasberg, MD

From the *Section of Hepatobiliary-Pancreatic Surgery, Department of Surgery, and the †Department of Radiology, Washington University School of Medicine, St. Louis, Missouri

Does Every Patient need it? Probably Not.

Is it still Relevant today? Absolutely.
Our job is to ask two questions…

Should we do it?
The Cadillac of Operations
The Family of High-Acuity

- Esophagectomy
- Pulmonary Resection
- Liver Resection
- APR
- AAA
- Liver Transplantation
High-Acuity Surgery

Hurdles

Co-morbidities
- Diabetes
- Metabolic Syndrome: HTN, Obesity

Its CANCER
- Immunosuppression
- Prothrombotic state
- Malnutrition

Age…
Should we offer this operation for the Elderly?

Benchmark operative standards and postoperative outcomes for the non-elderly resections can be matched in elderly patients despite higher preoperative acuity. Actual surgical performance is on par.

Postoperative survival is diminished in the elderly on account of decreased expected life-span and a greater proportion of resections being performed for malignancy.

Severe complications, although infrequent, take a more significant toll on the elderly.

Pancreatic resections in the elderly accrue greater costs, including the “hidden” implications of complications and rehabilitation care.
Prediction Models

• ASA
• Charlson
• POSSUM
• NSQIP
• Hopkins
• FOTB
Beware!

$O_2$ Prongs
Wheelchairs
Cirrhosis
Dementia
Our job is to ask two questions...

Should we do it?
Why Surgery?

- Resection is possible in only 20% of patients
- Usually limited to lesions in the pancreatic head
  (10% of tumors are in the body/tail)
- Operative mortality rates: 2-4%
- 5-year survival after resection ranges from 15 - 30%
- For unresectable patients, median survival = 6 mo
Underutilization of Surgery

28.6% of Clinical Stage 1 received surgery!!!!!!!!!!!!

- Most were resectable (96%)

Why so few????

- Unidentified Reason (52%)
  - 38% Not offered & 14% unknown
- Refused Surgery (4%)
- Contraindications (9%)
- Comorbidities (6%)

Predictors

- Medicare, Older, Black, Lower income, Less educated, Head Lesions, LV/Community Hospitals

Who Should Do This Stuff?

Morbidity, mortality, LOS and costs are lower at HV centers

Medicare claims database study of 7,229 pts age >65
- Pancreaticoduodenectomy for benign and malignant disease
- > 50% of patients had operation at lowest volume hospitals

<table>
<thead>
<tr>
<th>Hospital volume</th>
<th>Very low (&lt;1/yr)</th>
<th>Low (1-2/yr)</th>
<th>Medium (2-5/yr)</th>
<th>High (&gt;5/y)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mortality</td>
<td>16%</td>
<td>12%</td>
<td>10%</td>
<td>4%</td>
</tr>
<tr>
<td>3-year survival</td>
<td>25%</td>
<td>26%</td>
<td>29%</td>
<td>37%</td>
</tr>
</tbody>
</table>

Birkmeyer JD et al, *Surgery* 1999
Pancreatic Surgery

Who Is This Man?

Professor Allen Oldfather Whipple

Columbia Presbyterian Hospital

New York City 1935

Halstead Ampullary Resection

Three Stages
The Whipple Procedure

- GI Disconnection
- Biliary Disconnection
- Pancreatic Disconnection
- Lymphadenectomy
- Fierce Vascular Disconnection
- Reconstruction
R Status: The Basics

Represents *residual* disease at resection margins

R0: Grossly complete, microscopically negative

R1: Grossly complete, microscopically positive

R2: Grossly incomplete resection
Margin Definitions

Whipple and Total Pancreatectomy

- Radial
  - Posterior
  - Anterior
- Stomach/Duodenum
- Jejunum
- Bile Duct
- Pancreatic Neck
The Problem Child

Retroperitoneal?/Uncinate?/Mesenteric?/SMA?
Posterior Resection Margin: Uncinate Process off SMA

Portal Vein

SMV

Superior Mesenteric Artery

* *
It’s All About The Reconstruction
The Reconstruction
The Reconstruction
Afferent Limb Reconstruction
- Pancreaticojejunostomy
- Hepaticojejunostomy
- Duodenojejunostomy

Common Hepatic Duct

Pancreatic Anastomosis
Today’s Whipple Procedure

• Safer than ever – esp. high volume centers
• As ineffective as ever against cancer
• Operative Mortality 1-2%
• Morbidity 20-25%
  – Anastomotic Leak/Fistula – 15%
• Long-Term Recovery
  – 3 Months
  – Diabetes (25%)
  – Exocrine Insufficiency (25%)

*Ultimately, the quality of life (and palliation) is quite good, overall*
A Team Sport

- Interventional Endoscopy
- Pathology
- Radiology
- Medical Pancreatology
- Anesthesia
- Critical Care
- Interventional Radiology
- Nursing
Penn Outcomes

• Operability = Resectability
• Time...5-6 hours

• Leaks: 15%
• Reoperation: 6%
• ICU use: 9%
• Transfusion Rate: 13%
• Death: 1.5%
• LOS: Average 7 - 8 days
• Readmission Rate: 18%
• Cost: $20,000 per patient

• Simplify: Clinical Pathway
  – (2/3 follow on course)
Your Pathway To Recovery From Pancreatic Surgery

<table>
<thead>
<tr>
<th>Day of Operation</th>
<th>POD #1</th>
<th>POD #2</th>
<th>POD #3</th>
<th>POD #4</th>
<th>POD #5</th>
<th>POD #6</th>
<th>POD #7+</th>
<th>Discharge</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Labs</strong></td>
<td>CBC</td>
<td>CBC</td>
<td>N/A</td>
<td>N/A</td>
<td>CBC</td>
<td>N/A</td>
<td>N/A</td>
<td>N/A</td>
</tr>
<tr>
<td><strong>Pain Control</strong></td>
<td>Epidural/Analgesia or Pain Team Consultation</td>
<td>Epidural/Analgesia or Pain Team Consultation</td>
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<td><strong>Medications</strong></td>
<td>Anticoagulation: SQ Heparin 5000 qh</td>
<td>Heparin 5000 SQ qh</td>
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</tr>
<tr>
<td><strong>Fluid/Intake</strong></td>
<td>Fluids: PO q6h</td>
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<td><strong>Antibiotics</strong></td>
<td>Pre-operative Aminoglycoside</td>
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<tr>
<td><strong>Nutrition</strong></td>
<td>NPO</td>
<td>NPO</td>
<td>NPO</td>
<td>NPO</td>
<td>NPO</td>
<td>NPO</td>
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</tr>
<tr>
<td><strong>Endocrine</strong></td>
<td>Fingertips q4h</td>
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</tr>
<tr>
<td><strong>Tubes, Drains, &amp; Lines</strong></td>
<td>NG Tube</td>
<td>NG Tube</td>
<td>NG Tube</td>
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<tr>
<td><strong>Activity</strong></td>
<td>Bedrest</td>
<td>Out of bed to chair</td>
<td>Work with PT/OT</td>
<td>Work with PT/OT</td>
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**Discharge**
- Pain Control: Oral Dilaudid or Percocet + Tylenol or Ibuprofen
- Medications: Bowel Regimen: Clear liquids for 2-3 days (If percutaneous drains stay >4 weeks)
- Antibiotics: As needed for acquired infections
- Diet: Regular meals plus nutrition shakes (smaller, more frequent meals)
- Respiratory: Use your incentive spirometer at home
- Diabetes Management: +/- Glucagon Supplemental insulin, as needed
- Wound Care: Packing, if necessary
- Drain Care: Peristomal stoma to gravity bag (If necessary)
- Activity: Frequent walking

**Upper Abdominal Anatomy**

**Whipple Reconstruction**

**Distal Resection**

**Double Bypass**
Natural Progression of Pancreatic Cancer

Median survival 18 months with surgery alone

Following surgery:

- 50-80% local recurrence rate
- 25-50% distant metastases (liver and peritoneal)

So, can we improve on this?
Johns Hopkins Experience

- 4 yr follow up of 174 pts
- Not randomized
- Adjuvant therapy of 5-FU and XRT
- Median survival of 13.5 months (control) vs. 19.5 months (treated)

Yeo CJ et al, Ann Surg 1997
GEMCITABINE VS 5-FU for Advanced Disease

Log-Rank Test
\( p = 0.0009 \)

Median Survival:
Gemcitabine 5.65 mo
5-FU 4.41 months
\( p = 0.0025 \)

Burris et al, JCO 1997
Survival at Penn

- 1 yr survival: 76%
- ACTUAL 5-yr survival: 21%
- 5 yr survival: 23%
# Predictors of Survival

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<th>Intraop</th>
<th>Postop</th>
<th>Pathology</th>
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<td>Coagulopathy</td>
<td>Blood Loss</td>
<td>ICU Admission</td>
<td>Differentiation</td>
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<td>Dementia</td>
<td>Blood Transfusion</td>
<td>Duration of Stay</td>
<td>Tumor Size</td>
</tr>
<tr>
<td>POSSUM Physiology</td>
<td>Margins</td>
<td>Sepsis</td>
<td>T-Stage</td>
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<td>Charlson Score</td>
<td>POSSUM Operative</td>
<td>Ulcer</td>
<td>N-Stage</td>
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<td>ASA Score</td>
<td>Adjuvant Therapy</td>
<td># Positive Nodes</td>
<td></td>
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<tr>
<td></td>
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<td>LN ratio</td>
<td></td>
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<td></td>
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<td>AJCC Stage</td>
<td></td>
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Cox Proportional Hazards Model
It’s a Systemic Disease
# The Five Most Common Solid Tumors 2006

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We are Lagging Behind By 20-30 Years
Why???

• It’s relative rarity.
• It’s not discoverable.
• It’s biology is clearly different.
• It’s not pretty.

• Who’s treating it?
• Who’s studying it?
• Who’s funding it?
Satisfaction of a Cancer Survivor