Surgical Management of Pancreatic Cancer

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## Estimated New Cancer Deaths By Sex
United States, 2011

<table>
<thead>
<tr>
<th>Site</th>
<th>Males</th>
<th>Females</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung &amp; bronchus</td>
<td>85,600 28%</td>
<td>71,340 26%</td>
</tr>
<tr>
<td>Prostate</td>
<td>33,720 11%</td>
<td>39,520 15%</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>25,250 8%</td>
<td>24,130 9%</td>
</tr>
<tr>
<td>Pancreas</td>
<td>19,360 6%</td>
<td>18,300 7%</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>13,260 4%</td>
<td>15,460 6%</td>
</tr>
<tr>
<td>Leukemia</td>
<td>12,740 4%</td>
<td>9,570 4%</td>
</tr>
<tr>
<td>Esophagus</td>
<td>11,910 4%</td>
<td>9,040 3%</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>10,670 4%</td>
<td>8,120 3%</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>9,750 3%</td>
<td>6,330 2%</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>8,270 3%</td>
<td>5,670 2%</td>
</tr>
<tr>
<td><strong>All Sites</strong></td>
<td><strong>300,430 100%</strong></td>
<td><strong>271,520 100%</strong></td>
</tr>
</tbody>
</table>

Source: CA Cancer J Clin 2011;61:212-236
Pancreatic Cancer

- Only 15-20% of patients with pancreatic cancer are resectable.
- 50% have metastatic disease at presentation.
- Median survival:
  - R0 resection ~ 20 months
  - Locally advanced unresectable ~ 12 months
  - Metastatic disease ~ 4-6 months
- Optimal therapy pancreatic cancer remains controversial.
History

• Walter Kausch (1909), a German surgeon from Berlin, performed the first “successful” PD in a two-stage operation. The patient had an ampullary adenocarcinoma and lived for 9 months.

• George Hirschel (1914, a German surgeon from Heidelberg) and Ottorino Tenani (1922, an Italian surgeon from Bellagio) performed successful PDs for ampullary tumors.

• Allan O. Whipple (1935) was the first American to perform a PD and reported the first series of PDs at the annual American Surgical Association meeting.
1960’s – 1970’s

- High perioperative morbidity
- Hospital mortality ~ 25%
- Long term survival for pancreatic cancer ~ 5%
- Calls to abandon PD for pancreatic cancer
Pancreateicoduodenectomy for Pancreatic Cancer at Johns Hopkins
# Pancreaticoduodenectomy for Pancreatic Cancer at Johns Hopkins

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
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</tr>
</thead>
<tbody>
<tr>
<td>Patients</td>
<td>41</td>
<td>47</td>
<td>1173</td>
</tr>
<tr>
<td>Pylorus preserving</td>
<td>0</td>
<td>30%</td>
<td>67.8%</td>
</tr>
<tr>
<td>Blood loss</td>
<td>3200 ml</td>
<td>1700 ml</td>
<td>927 ml</td>
</tr>
<tr>
<td>Transfusions</td>
<td>6.3 U</td>
<td>3.6 U</td>
<td>0.83 U</td>
</tr>
<tr>
<td>Op time</td>
<td>9.0 hr</td>
<td>7.8 hr</td>
<td>6.3 hr</td>
</tr>
<tr>
<td>Mortality</td>
<td>24%</td>
<td>2%</td>
<td>0.7%</td>
</tr>
<tr>
<td>Op/year</td>
<td>3.4</td>
<td>7.8</td>
<td>112.4</td>
</tr>
</tbody>
</table>
Long-term Survival of Patients Who Underwent PD for Pancreatic Cancer, by Histologic Type

Ductal adenocarcinoma, n=1175

Neuroendocrine carcinoma, n=98

IPMN with invasive cancer, n=90
Long-term Survival for Ductal Adenocarcinoma of the Pancreas

**Tumor Diameter**
- $< 3$ cm
- $\geq 3$ cm

**Lymph Node Status**
- no positive nodes
- positive nodes

**Margin Status**
- negative margin
- positive margin

**Histologic Grade**
- well or moderate
- poor or undifferentiated

$p<0.0001$
# Predictors of Long-term Survival: Multivariate Analysis

<table>
<thead>
<tr>
<th>Risk factor</th>
<th>Hazard Ratio</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Tumor diameter (≥3 cm)</td>
<td>1.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Positive lymph nodes</td>
<td>1.3</td>
<td>0.05</td>
</tr>
<tr>
<td>Resection margin status</td>
<td>1.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Histological grade (poorly or undifferentiated)</td>
<td>1.6</td>
<td>&lt;0.001</td>
</tr>
<tr>
<td>Adjuvant therapy</td>
<td>0.5</td>
<td>&lt;0.001</td>
</tr>
</tbody>
</table>
Long-term Survival of Patients Undergoing PD for Ductal Adenocarcinoma of the Pancreas, by Decade

Proportion Surviving

months

Proportion Surviving

n=23 n=65

n=573 n=514

1970s 1980s

1990s 2000s
Summary of Hopkins Surgical Experience (2013)

- ~2000 PDs for pancreatic cancer, >70% for ductal adenocarcinoma
- The median patient age has increased over time
- Three-quarters of patients presented with jaundice; most had their biliary tract decompressed prior to PD
- Perioperative mortality has decreased to ~1% but perioperative morbidity remains high (~40%)
- The postoperative length of stay has decreased over time
- Pathologic features of the cancer are important determinants of long-term survival
- Long-term survival has increased over time
Adjusted Relative Risk of In-Hospital Mortality By Procedure & Hospital Volume

* \( p<0.05; \) ** \( p<0.01; \) *** \( p<0.001 \) for comparison to the high volume reference group.
## Volume Effects on Long-Term Survival

<table>
<thead>
<tr>
<th>Volume</th>
<th>3 year Survival</th>
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<tbody>
<tr>
<td>Very Low</td>
<td>25%</td>
</tr>
<tr>
<td>Low</td>
<td>26%</td>
</tr>
<tr>
<td>Medium</td>
<td>29%</td>
</tr>
<tr>
<td>High</td>
<td>37%</td>
</tr>
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</table>

(adjusted Hazard ratio 0.69, 95% CI 0.62-0.76)

Surgery (1999)
Multidisciplinary Clinic for the Management of Pancreatic Cancer at Johns Hopkins

- Patients triaged by need for multidisciplinary consultation.
- Standardized assessment, pathology review, imaging review, Multi-D conference, discussion.
- Support services (nutrition, nursing, social work, National Familial Registry, Pain service).
Pancreatic Cancer: Determining Local Resectability

Historic Method

- Duodenum
- Tumor
- Superior Mesenteric V.
- Superior Mesenteric A.
- Aorta
- Inferior Vena Cava

Current Method
Definitions

**Resectable:**
no extension to celiac, CHA, SMA

**Locally Advanced:**
celiac, SMA encasement (> 180°)
stage III (T4, Nx, M0)

**Borderline:**
SMV-PV abutment or short segment encasement
Abutting SMA (<180°)
Short segment abutment/encasement of the CHA/PHA (typically at GDA origin)
Resectable
Borderline Resectable

SMV-PV Involvement

Arterial Abutment
Locally Advanced (Unresectable)
Management Paradigms Based on Local Extent if Disease

Resectable
- Resection → post-op CT or CRT
- Neoadjuvant controversial

Locally Advanced
- Unresectable
- Chemoradiation therapy
- Consider chemotherapy alone

Borderline
- Preoperative CRT
- Vascular resection
Imaging and Staging of Pancreatic Adenocarcinoma

Limitations of Imaging Studies

- Small Volume Peritoneal Disease
- Small Hepatic Metastasis
- Extent of Vein Involvement Versus Contact
Extending Limits of Surgical Therapy: Rationale for PD with Vascular Resection

- Involvement of the SMV-PV can often be predicted or suspected by preoperative CT criteria

- No biologic difference between a large vein and a small vein

- It is possible to achieve an R0 resection in patients with tumor extension to the SMV-PV
SMV-PV Reconstruction: Classification

V1

V2

V3

V4

V5

Tseng, J Gastroint Surg 2004;8:935.
Vascular Reconstruction
<table>
<thead>
<tr>
<th>Variable</th>
<th>No. patients</th>
<th>Median survival (mo)</th>
<th>95% CI</th>
<th>P value</th>
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<tbody>
<tr>
<td>Overall</td>
<td>291</td>
<td>24.9</td>
<td>21.40-28.46</td>
<td>--</td>
</tr>
<tr>
<td>Male</td>
<td>175</td>
<td>23.1</td>
<td>19.05-27.15</td>
<td>.47</td>
</tr>
<tr>
<td>Female</td>
<td>116</td>
<td>27.0</td>
<td>22.43-31.50</td>
<td></td>
</tr>
<tr>
<td>Standard PD</td>
<td>181</td>
<td>26.5</td>
<td>21.1-31.89</td>
<td>.18</td>
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<tr>
<td>PD with VR</td>
<td>110</td>
<td>23.4</td>
<td>19.50-27.37</td>
<td></td>
</tr>
<tr>
<td>T1</td>
<td>25</td>
<td>30.8</td>
<td>16.61-44.92</td>
<td>.22</td>
</tr>
<tr>
<td>T2</td>
<td>56</td>
<td>25.9</td>
<td>20.2-31.46</td>
<td></td>
</tr>
<tr>
<td>T3</td>
<td>206</td>
<td>23.7</td>
<td>19.94-27.46</td>
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<tr>
<td>N0</td>
<td>146</td>
<td>31.9</td>
<td>24.57-39.30</td>
<td>.005</td>
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<tr>
<td>N1</td>
<td>145</td>
<td>21.1</td>
<td>17.40-24.73</td>
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<tr>
<td>R0</td>
<td>246</td>
<td>26.5</td>
<td>22.29-30.71</td>
<td>.14</td>
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<tr>
<td>R1</td>
<td>45</td>
<td>21.4</td>
<td>17.05-25.68</td>
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<td>Adjuvant therapy</td>
<td>209</td>
<td>25.1</td>
<td>21.42-28.85</td>
<td>.92</td>
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<tr>
<td>No adj therapy</td>
<td>29</td>
<td>18.5</td>
<td>9.48-27.52</td>
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</tbody>
</table>

Tseng, J Gastroint Surg 2004;8:935.
Goals of Adjuvant/Neoadjuvant Therapy for Resectable Pancreatic Cancer

• Improve survival

• Decrease local recurrence
  – Requires adequate surgical resection (R0 vs R1)
  – What is the role/contribution of radiation therapy?

• Prevent/delay distant recurrence
  – Chemotherapy

• May avoid surgery in those at risk for early failure (neoadjuvant therapy)
Situations to Consider Neoadjuvant Therapy

1. Technically Borderline
   - Arterial abutment
   - Venous involvement

2. Oncological concern for advanced disease
   - CA 19-9 >1000
   - Indeterminate liver lesion

3. Compromised performance status or co-morbid disease
Surgical resection for pancreatic cancer is being performed with increasing frequency in the U.S. and worldwide.

Pancreatic resection can be performed safely in centers with experience.

High quality preoperative imaging and multidisciplinary management is important.

Attention to achieving negative margins is important, incorporating vascular resection and reconstruction as needed.

While adjuvant therapy improves outcomes, the optimal regimen, timing, and role of RT remain controversial.