Pancreatic cancer: What defines resectability and the role for surgery

Douglas B. Evans
For the Multidisciplinary Pancreatic Cancer Study Group
The University of Texas
M. D. Anderson Cancer Center
Houston, Texas
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# Multidisciplinary Clinical Working Group

**Surgery**  
Peter Pisters  
Jeff Lee  
Jason Fleming  
Nick Vauthey  
Eddie Abdalla

**Medical Oncology**  
Jim Abbruzzese  
Robert Wolff  
Gauri Varadhachary  
Mike Fisch  
Milind Javle  
David Fogelman

**Radiation Oncology**  
Chris Crane  
Sunil Krishnan  
Prajnan Das

**Pathology**  
Huamin Wang  
Gregg Staerke

**Diagnostic Imaging**  
Eric Tamm  
Chusilp Charnsangavej  
Lisa Lano  
Priya Bhosale  
Aparna Balachandran

**Gastroenterology**  
Jeffrey H. Lee  
Manoop Bhutani
## Stage-specific survival

<table>
<thead>
<tr>
<th>Stage</th>
<th>Months From Dx</th>
</tr>
</thead>
<tbody>
<tr>
<td>All patients</td>
<td>9.3</td>
</tr>
<tr>
<td>Stage I, II</td>
<td>15.4</td>
</tr>
<tr>
<td>resected</td>
<td>24.1</td>
</tr>
<tr>
<td>not resected</td>
<td>10.3</td>
</tr>
<tr>
<td>Stage III</td>
<td>9.9</td>
</tr>
<tr>
<td>borderline</td>
<td>17.6</td>
</tr>
<tr>
<td>Stage IV</td>
<td>6.1</td>
</tr>
</tbody>
</table>

Katz MHG, Hwang RF, et al. TNM staging of pancreatic adenocarcinoma.
• Inaccurate
• Incomplete gross resection provides no survival benefit compared to chemoradiation without surgery
## Complete Resection

### R Status

<table>
<thead>
<tr>
<th>R Designation</th>
<th>Gross Resection</th>
<th>Microscopic Margin</th>
</tr>
</thead>
<tbody>
<tr>
<td>R0</td>
<td>complete</td>
<td>negative</td>
</tr>
<tr>
<td>R1</td>
<td>complete</td>
<td>positive</td>
</tr>
<tr>
<td>R2</td>
<td>incomplete</td>
<td>positive</td>
</tr>
</tbody>
</table>

SMA (Retroperitoneal) Margin
SYNOPTIC REPORT
Specimen: Pancreaticoduodenectomy
Tumor Diagnosis: DUCTAL ADENOCARCINOMA
Degree of Differentiation: Moderate
The tumor size is 2.8 cm in diameter
Extrapancreatic extension present
Lymphovascular present
Perineural invasion present
**SMA margin uninvolved** with distance of 18mm to inked margin
Bile duct margin uninvolved
Pancreatic transection margin uninvolved
Proximal stomach or duodenum margin uninvolved
Distal duodenum or jejunum margin uninvolved
Regional Lymph Nodes:
  - **Total number involved:** 3
  - **Total number examined:** 30, including hepatic artery and periaortic (Parts A and B)
Vessels removed: None stated
Final pTNM Staging (AJCC 6th edition):
  - **pT3** Tumor extends beyond the pancreas
  - **pN1** Regional lymph node metastasis
  - **pMX** Distant metastasis cannot be assessed
Definitions

Resectable:
no extension to celiac, CHA, SMA
patent SMV-PV confluence
stage I, II (T1-3, Nx, M0)

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

Borderline:
artrial abutment (≤ 180°)
stage III (minimal T4)

Resectable

Borderline Resectable

Locally Advanced

Courtesy of R Wolff, MD
<table>
<thead>
<tr>
<th></th>
<th>SMV</th>
<th>SMA</th>
</tr>
</thead>
<tbody>
<tr>
<td>Surrounding perineural plexus</td>
<td>NO</td>
<td>YES</td>
</tr>
<tr>
<td>Resection operative risk</td>
<td>Low</td>
<td>High</td>
</tr>
<tr>
<td>If resect, is the resection complete (R0)</td>
<td>Usually</td>
<td>Usually not</td>
</tr>
</tbody>
</table>

**Diagram:**
- Portal vein
- SMV
- SMA
- Inferior pancreaticoduodenal artery
- SMA
Resectable adenocarcinoma of the pancreatic head

SMV

SMA

T

Kitts 527268

Resectable tumor, RRHA
Resectable: likely to require venous resection
Resectable: likely to require venous resection
Borderline Resectable


Locally Advanced (Stage III)
Locally Advanced (Stage III)

Celiac encasement

SMA encasement
Definitions: SSO/AHPBA CC

Resectable:
no extension to celiac, CHA, SMA, SMV-PV confluence
stage I, II (T1-3, Nx, M0)

Borderline:
a) venous abutment or encasement (with option for reconstruction)
b) arterial abutment (≤ 180°)

Locally Advanced:
celiac, SMA encasement (> 180°)
stage III (T4, Nx, M0)
Imaging Template for Pancreatic Cancer

- Tumor size and location
- Tumor and veins relationship – SMV, portal vein and splenic vein
- Tumor and arteries relationship – SMA, celiac axis, common hepatic artery
- Presence or absence of distant metastases – liver, lung, peritoneum

MDACC Multidisciplinary Pancreatic Cancer Study Group
MDACC Classification System for Borderline Resectable Disease

• Type A: Anatomically *borderline* resectable tumor (tumor abuts artery for $\leq 180^0$)

• Type B: *Indeterminant* extrapancreatic metastasis

• Type C: Patient of *marginal* performance status

Treatment of Borderline Resectable Pancreatic Cancer

Underlying hypothesis / assumption

1. Neoadjuvant treatment sequencing used to:
   - select those with favorable biology
   - treat radiographically occult M1 disease
   - enhance the chance of a complete (R0, R1) resection

2. Outcome for R1 different than R2 (ie, better)
## Accurate Pathology and Multimodality Therapy

**Pancreaticoduodenectomy: Ductal Adenocarcinoma**  
**M D Anderson (N = 360)**

<table>
<thead>
<tr>
<th>Variable</th>
<th>No. Pts</th>
<th>Med Sur</th>
<th>p value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Overall</td>
<td>360</td>
<td>25</td>
<td></td>
</tr>
<tr>
<td>N0</td>
<td>174</td>
<td>32</td>
<td>.002</td>
</tr>
<tr>
<td>N1</td>
<td>186</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>R0</td>
<td>300</td>
<td>28</td>
<td></td>
</tr>
<tr>
<td>R1</td>
<td>60</td>
<td>22</td>
<td></td>
</tr>
<tr>
<td>Maj Comp</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>No</td>
<td>263</td>
<td>27</td>
<td></td>
</tr>
<tr>
<td>Yes</td>
<td>93</td>
<td>22</td>
<td></td>
</tr>
</tbody>
</table>

R0  17 mo  
R1  11 mo  

ESPAC-1  
Ann Surg 2001

Local Failure (All pts): 8%

Raut, Ann Surg 2007;246:52-60
The Importance of Neoadjuvant Therapy
Pancreaticoduodenectomy: Ductal Adenocarcinoma
M D Anderson (N = 360)

<table>
<thead>
<tr>
<th>Preoperative Therapy</th>
<th>R1 Resection</th>
</tr>
</thead>
<tbody>
<tr>
<td>YES</td>
<td>13%</td>
</tr>
<tr>
<td>NO</td>
<td>19%</td>
</tr>
</tbody>
</table>

Raut, Ann Surg 2007;246:52-60
Local Failure (All pts): 8%
Borderline Resectable PC
MDACC Treatment Approach

- Treatment phase
- Break ~ 6 wks

- CTX gem combo
- Chemo-XRT

- Restaging
- Dropout

- Classification as Borderline
- Restaging
- Dropout

## Rates of Resection, Path Response, Survival
160 Patients with Borderline Resectable PC

<table>
<thead>
<tr>
<th>MDACC Type</th>
<th>No. of Patients (%)</th>
<th>Median Survival (Mos)</th>
<th>p*</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
<td>Total</td>
<td>Resected</td>
<td>Path Resp. IIb, III, IV</td>
</tr>
<tr>
<td>A</td>
<td>84 (53)</td>
<td>32 (38)</td>
<td>19 (59)</td>
</tr>
<tr>
<td>B</td>
<td>44 (28)</td>
<td>22 (50)</td>
<td>13 (59)</td>
</tr>
<tr>
<td>C</td>
<td>32 (20)</td>
<td>12 (38)</td>
<td>5 (42)</td>
</tr>
<tr>
<td>Total</td>
<td>160</td>
<td>66 (41)</td>
<td>37 (56)</td>
</tr>
</tbody>
</table>

*p: comparison of median survival between resected and unresected patients of each type

Final path:
R0
Lymph nodes: 0/24

Rev saph vein graft

divided bile duct

saph vein patch

CHA

PV

Spl A

Spl V

SMV

492495
Summary

- Local tumor resectability is best determined by high quality CT (exploratory surgery is outdated)

- Resectable tumors may be treated with upfront surgery or a neoadjuvant approach

- Borderline resectable tumors are best treated with upfront systemic therapy/chemoradiation

- Locally advanced tumors, as defined by arterial encasement, are not resectable and surgery is not a realistic treatment option