Management of Borderline - Resectable Pancreatic Cancer

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Medical Director of the Hollings Cancer Center
The Medical University of South Carolina
### Estimated Cancer Deaths in the US in 2013

<table>
<thead>
<tr>
<th>Cancer Type</th>
<th>% of Deaths</th>
<th>Deaths</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung &amp; bronchus</td>
<td>28%</td>
<td>306,920</td>
</tr>
<tr>
<td>Prostate</td>
<td>10%</td>
<td></td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>9%</td>
<td></td>
</tr>
<tr>
<td>Pancreas</td>
<td>6%</td>
<td></td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>5%</td>
<td></td>
</tr>
<tr>
<td>Leukemia</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>Esophagus</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>All other sites</td>
<td>24%</td>
<td></td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>26%</td>
<td>273,430</td>
</tr>
<tr>
<td>Breast</td>
<td>14%</td>
<td></td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>9%</td>
<td></td>
</tr>
<tr>
<td>Pancreas</td>
<td>7%</td>
<td></td>
</tr>
<tr>
<td>Ovary</td>
<td>5%</td>
<td></td>
</tr>
<tr>
<td>Leukemia</td>
<td>4%</td>
<td></td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>Uterine corpus</td>
<td>3%</td>
<td></td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>2%</td>
<td></td>
</tr>
<tr>
<td>Brain/other nervous system</td>
<td>2%</td>
<td></td>
</tr>
<tr>
<td>All other sites</td>
<td>25%</td>
<td></td>
</tr>
</tbody>
</table>
## Trends in Five-year Relative Cancer Survival Rates (%), 1975-2008

<table>
<thead>
<tr>
<th></th>
<th></th>
<th></th>
<th></th>
</tr>
</thead>
<tbody>
<tr>
<td>All sites</td>
<td>49</td>
<td>56</td>
<td>68</td>
</tr>
<tr>
<td>Breast (female)</td>
<td>75</td>
<td>84</td>
<td>90</td>
</tr>
<tr>
<td>Colon</td>
<td>51</td>
<td>61</td>
<td>65</td>
</tr>
<tr>
<td>Leukemia</td>
<td>34</td>
<td>43</td>
<td>58</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>12</td>
<td>13</td>
<td>17</td>
</tr>
<tr>
<td>Melanoma</td>
<td>82</td>
<td>88</td>
<td>93</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>47</td>
<td>51</td>
<td>71</td>
</tr>
<tr>
<td>Ovary</td>
<td>36</td>
<td>38</td>
<td>43</td>
</tr>
<tr>
<td>Pancreas</td>
<td>2</td>
<td>4</td>
<td>6</td>
</tr>
<tr>
<td>Prostate</td>
<td>68</td>
<td>83</td>
<td>100</td>
</tr>
<tr>
<td>Rectum</td>
<td>48</td>
<td>58</td>
<td>68</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>73</td>
<td>79</td>
<td>80</td>
</tr>
</tbody>
</table>

5-year relative survival rates based on patients diagnosed from 2002 to 2008, all followed through 2009.
### Resection (R) Status

<table>
<thead>
<tr>
<th>R Designation</th>
<th>Gross Margin</th>
<th>Microscopic Margin</th>
</tr>
</thead>
<tbody>
<tr>
<td>R0</td>
<td>Negative</td>
<td>Negative</td>
</tr>
<tr>
<td>R1</td>
<td>Negative</td>
<td>Positive</td>
</tr>
<tr>
<td>R2</td>
<td>Positive</td>
<td>Positive</td>
</tr>
</tbody>
</table>
Resectable

- No distant metastases
- No SMV or PV distortion
- Fat planes around celiac axis, hepatic artery, and SMA
Locally Advanced

- Encasement ($\geq 180^\circ$) of celiac, CHA, or SMA
- Extensive occlusion of SMV/PV
  - Not amenable to resection/reconstruction
Borderline - Resectable

- No distant metastases
- Venous involvement of the SMV or PV with suitable vessels for reconstruction
- Gastroduodenal artery encasement up to the hepatic artery
- Tumor abutment of the SMA (<180°)
Clinical/Radiologic Staging → Treatment

• **Localized**
  - Surgery
  - Adjuvant chemotherapy
  - +/- Adjuvant chemoXRT

• **Borderline Resectable**
  - Surgery
  - Neoadjuvant therapy (chemo OR chemoXRT)
  - +/- Adjuvant chemotherapy

• **Locally Advanced**
  - Chemotherapy +/- chemoXRT
Management of Borderline Resectable Lesions

- Limited evidence supporting specific neoadjuvant regimens off-study
- Practices vary regarding neoadjuvant chemotherapy and chemoradiation
- Performing surgery with a high likelihood of a positive margin is not recommended
BORDERLINE RESECTABLE\superscript{d,e} NO METASTASES, PLANNED RESECTION

**WORKUP**

**Planned Resection\superscript{f}** → Laparotomy → Surgical resection\superscript{f}

- Unresectable at surgery\superscript{f,j}
  - Biopsy confirmation of adenocarcinoma, if not performed previously
  - If appropriate, consider duodenal bypass (category 2B for prophylactic duodenal bypass) ± open ethanol celiac plexus block (category 2B)

- No jaundice
  - Stenting or biliary bypass ± duodenal bypass (category 2B for prophylactic duodenal bypass) ± open ethanol celiac plexus block when indicated by pain

- Jaundice
  - See Adjuvant Treatment and Surveillance (PANC-6)
  - See Locally Advanced Unresectable (PANC-7)
  - See Metastatic Disease (PANC-9)

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There is limited evidence to recommend specific neoadjuvant regimens off-study, and practices vary with regard to the use of chemotherapy and chemoradiation. Most NCCN institutions prefer neoadjuvant therapy at a high-volume center. Performing surgery with a high likelihood of a positive margin is not recommended.
BORDERLINE RESECTABLE\textsuperscript{d,e} NO METASTASES, PLANNED NEOADJUVANT THERAPY

WORKUP

- Biopsy positive → Neoadjuvant therapy
- Biopsy, EUS with FNA preferred\textsuperscript{k}
- Consider staging laparoscopy\textsuperscript{l}
- Placement of stent (preferably a short metal stent) if biliary ductal obstruction is present

Planned neoadjuvant therapy\textsuperscript{h}

Cancer not confirmed → Repeat biopsy

Cancer not confirmed (exclude autoimmune pancreatitis [AIP]) → See Planned Resection (PANC-5)

Biopsy positive → Neoadjuvant therapy (follow pathway above)\textsuperscript{j}

Disease progression precluding surgery\textsuperscript{j}
- See Locally Advanced Unresectable (PANC-7) or Metastatic Disease (PANC-9)

Jaundice
- Disease progression precluding surgery\textsuperscript{j}
  - See Locally Advanced Unresectable (PANC-7) or Metastatic Disease (PANC-9)
- Jaundice
  - Stenting or biliary bypass ± duodenal bypass (category 2B for prophylactic duodenal bypass)
  - ± open ethanol celiac plexus block (category 2B)

No jaundice
- Unresectable at surgery\textsuperscript{f,j}
  - See Locally Advanced Unresectable (PANC-7)

Surgical resection\textsuperscript{f}
- No jaundice
International Study Group of Pancreatic Surgery (ISGPS) On Borderline Lesions

- Exploration is recommended
- Venous resection & reconstruction when indicated & possible
- Arterial resection is not recommended for right-sided lesions
- Neoadjuvant strategies should be assessed in clinical trials
International Study Group of Pancreatic Surgery (ISGPS): Classification of Venous Resection

- Type 1: partial venous excision with closure
- Type 2: partial venous excision and patch
- Type 3: circumferential resection/anastomosis
- Type 4: circumferential resection/interposition
SMV/PV Resection & Type 4 Reconstruction
Pancreaticoduodenectomy in the Presence of Superior Mesenteric Venous Obstruction


(J GASTROINTEST SURG 2005;9:915–921)
Use of the Left Renal Vein as a Practical Conduit in Superior Mesenteric Vein Reconstruction

Haroon Choudry, M.D., Diego Avella, M.D., Luis Garcia, M.D., David Han, M.D.,
Kevin Staveley-O’Carroll, M.D., Ph.D.,¹ and Eric Kimchi, M.D.

Department of Surgery, Penn State University, Hershey, Pennsylvania
Neck/Body Lesions with Arterial Involvement
• 99 underwent resection of UGI/HPB malignancy and completed their postoperative chemotherapy at PSCI

• Quality of life was measured using FACIT-Sp

• UGI/HPB surgery patients had a higher self-reported QOL when compared to cancer patients who did not undergo surgical treatment

• Pancreatic surgery patients had the highest mean QOL scores among this group
Rationales for Neoadjuvant Therapy

- Evaluate biologic response or progression (local or distant)
- Potential for downstaging borderline resectable and potential to increase the rate of R0 resections
Neoadjuvant Treatment Algorithm

PHASE II STUDY FOR BORDERLINE PANCREATIC-HEAD ADENOCARCINOMA

Modified FOLFIRINOX Chemotherapy for 4 cycles (8 weeks)

↓

Stable or Tumor Response

↓

Capecitabine with Radiation
(4,500 cGy in 25 fractions over 5 weeks)

↓

Surgery

↓

Adjuvant Gemcitabine Chemotherapy for 6 months
Conclusion

• Three important concepts
Combined pancreaticoduodenectomy and extended right hemicolectomy: outcomes and indications

Eric T. Kimchi, Mehrdad Nikfarjam, Niraj J. Gusani, Diego M. Avella & Kevin F. Staveley-O'Carroll
Department of Surgery, Penn State Milton S. Hershey Medical Center, Penn State College of Medicine, Hershey, PA, USA

Combined Right Nephrectomy and Pancreaticoduodenectomy. Indications and Outcomes

Mehrdad Nikfarjam1, Niraj J Gusani1, Eric T Kimchi1, Rickhesvar P Mahraj2, Kevin F Staveley-O’Carroll1

Departments of 1Surgery and 2Radiology, Penn State Milton S. Hershey Medical Center, Penn State College of Medicine, Hershey, PA, USA

Additional Organ Resection Combined with Pancreaticoduodenectomy does not Increase Postoperative Morbidity and Mortality

Mehrdad Nikfarjam · Mandeep Sehmbey ·
Eric T. Kimchi · Niraj J. Gusani · Serene Shereef ·
Diego M. Avella · Kevin F. Staveley-O’Carroll
EMT and Dissemination Precede Pancreatic Tumor Formation

Andrew D. Rhim,1,3,4 Emily T. Mirek,1,3,4 Nicole M. Aiello,1,2,4 Anirban Maitra,6 Jennifer M. Bailey,6 Florencia McAllister,7 Maximilian Reichert,1,4 Gregory L. Beatty,3,4 Anil K. Rustgi,1,4 Robert H. Vonderheide,3,4 Steven D. Leach,5 and Ben Z. Stanger1,2,3,4,*

Figure 3. Hematogenous Spread and Liver Seeding Precede Tumor Formation
Thank you!

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