Surgical Advances for Pancreatic Cancer

September 26, 2018

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Herbert J Zeh, III, MD FACS
Professor and Chair of Surgery
Hall and Mary Lucile Shannon Distinguished Chair

September 26, 2018
Goals

- Review Current State of Pancreatic Cancer
- Discuss work up for potentially curable pancreatic cancer.
- Review Types of Pancreatic Surgery
- Discuss role of MIS approach to pancreatic surgery
- Explore Role of Surgery in Advanced Disease

Figure 3. Leading Sites of New Cancer Cases and Deaths – 2018 Estimates

<table>
<thead>
<tr>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Prostate</td>
<td>Breast</td>
</tr>
<tr>
<td>Lung &amp; bronchus</td>
<td>164,690</td>
</tr>
<tr>
<td>19%</td>
<td>266,120</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>121,680</td>
</tr>
<tr>
<td>14%</td>
<td>112,350</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>Colon &amp; rectum</td>
</tr>
<tr>
<td>75,610</td>
<td>64,640</td>
</tr>
<tr>
<td>9%</td>
<td>7%</td>
</tr>
<tr>
<td>Melanoma of the skin</td>
<td>Uterine corpus</td>
</tr>
<tr>
<td>62,380</td>
<td>63,230</td>
</tr>
<tr>
<td>7%</td>
<td>7%</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>Thyroid</td>
</tr>
<tr>
<td>56,150</td>
<td>40,900</td>
</tr>
<tr>
<td>6%</td>
<td>5%</td>
</tr>
<tr>
<td>Non-Hodgkin lymphoma</td>
<td>Melanoma of the skin</td>
</tr>
<tr>
<td>42,680</td>
<td>36,120</td>
</tr>
<tr>
<td>5%</td>
<td>4%</td>
</tr>
<tr>
<td>Oral cavity &amp; pharynx</td>
<td>Non-Hodgkin lymphoma</td>
</tr>
<tr>
<td>41,730</td>
<td>32,950</td>
</tr>
<tr>
<td>5%</td>
<td>4%</td>
</tr>
<tr>
<td>Leukemia</td>
<td>Pancreas</td>
</tr>
<tr>
<td>37,160</td>
<td>26,240</td>
</tr>
<tr>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>Leukemia</td>
</tr>
<tr>
<td>30,610</td>
<td>25,270</td>
</tr>
<tr>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>All sites</td>
<td>Kidney &amp; renal pelvis</td>
</tr>
<tr>
<td>856,370</td>
<td>22,660</td>
</tr>
<tr>
<td>100%</td>
<td>3%</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Male</th>
<th>Female</th>
</tr>
</thead>
<tbody>
<tr>
<td>Lung &amp; bronchus</td>
<td>Breast</td>
</tr>
<tr>
<td>83,550</td>
<td>70,500</td>
</tr>
<tr>
<td>26%</td>
<td>25%</td>
</tr>
<tr>
<td>Prostate</td>
<td>Breast</td>
</tr>
<tr>
<td>29,430</td>
<td>40,920</td>
</tr>
<tr>
<td>9%</td>
<td>14%</td>
</tr>
<tr>
<td>Colon &amp; rectum</td>
<td>Colon &amp; rectum</td>
</tr>
<tr>
<td>27,890</td>
<td>23,240</td>
</tr>
<tr>
<td>8%</td>
<td>8%</td>
</tr>
<tr>
<td>Pancreas</td>
<td>Pancreas</td>
</tr>
<tr>
<td>23,020</td>
<td>21,310</td>
</tr>
<tr>
<td>7%</td>
<td>7%</td>
</tr>
<tr>
<td>Liver &amp; intrahepatic bile duct</td>
<td>Liver &amp; intrahepatic bile duct</td>
</tr>
<tr>
<td>20,540</td>
<td>9,660</td>
</tr>
<tr>
<td>6%</td>
<td>3%</td>
</tr>
<tr>
<td>Leukemia</td>
<td>Non-Hodgkin lymphoma</td>
</tr>
<tr>
<td>14,270</td>
<td>8,400</td>
</tr>
<tr>
<td>4%</td>
<td>3%</td>
</tr>
<tr>
<td>Esophagus</td>
<td>Leukemia</td>
</tr>
<tr>
<td>12,850</td>
<td>10,100</td>
</tr>
<tr>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Urinary bladder</td>
<td>Leukemia</td>
</tr>
<tr>
<td>12,520</td>
<td>11,350</td>
</tr>
<tr>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Pancreas</td>
<td>Uterine corpus</td>
</tr>
<tr>
<td>11,510</td>
<td>11,350</td>
</tr>
<tr>
<td>4%</td>
<td>4%</td>
</tr>
<tr>
<td>Kidney &amp; renal pelvis</td>
<td>Pancreas</td>
</tr>
<tr>
<td>10,010</td>
<td>21,310</td>
</tr>
<tr>
<td>3%</td>
<td>7%</td>
</tr>
<tr>
<td>All sites</td>
<td>Leukemia</td>
</tr>
<tr>
<td>323,630</td>
<td>10,100</td>
</tr>
<tr>
<td>100%</td>
<td>4%</td>
</tr>
</tbody>
</table>

Estimated Deaths

- Estimates are rounded to the nearest 10, and cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder. Ranking is based on modeled projections and may differ from the most recent observed data.

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Tumors of the Pancreas – Usually Exocrine

- Head: 60-70%
- Neck/Body: 5-10%
- Tail: 10-15%
- Diffuse tumors involving entire gland: 20%

No histological difference between sites

- Carcinoma of the head: Obstructs bile duct, Ulcerates duodenal mucosa
- Carcinoma of the tail: Remains silent longer, Large & widely disseminated

Management Panc Ca

- Functional Staging of Pancreatic Cancer
  - Resectable Disease
    - Stage I, II
  - Borderline resectable
    - Stage IIB Stage III
  - Locally advanced
    - Stage III
  - Metastatic Disease
    - Stage IV

8th edition AJCC
for EPC

<table>
<thead>
<tr>
<th>Primary tumor (T)</th>
</tr>
</thead>
<tbody>
<tr>
<td>T1</td>
</tr>
<tr>
<td>T2</td>
</tr>
<tr>
<td>T3</td>
</tr>
<tr>
<td>T4</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Lymph nodes (N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>N0</td>
</tr>
<tr>
<td>N1</td>
</tr>
<tr>
<td>N2</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Metastases (M)</th>
</tr>
</thead>
<tbody>
<tr>
<td>M0</td>
</tr>
<tr>
<td>M1</td>
</tr>
</tbody>
</table>

<table>
<thead>
<tr>
<th>Stage</th>
<th>T1, N0, M0 (A)</th>
<th>T2, N0, M0 (B)</th>
<th>T3, N0, M0 (A)</th>
<th>T1–3, N1, M0 (B)</th>
<th>Any T, N2, M0</th>
<th>Any T, any N, M0</th>
<th>Any T, any N, M1</th>
</tr>
</thead>
</table>
Goals

- Review Current State of Pancreatic Cancer
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How do we define

1. resectable
2. borderline resectable
3. unresectable
   a. locally advanced
   b. metastatic
Standard Staging CT

Triphasic CT:
1. Arterial
2. Pancreatic
3. Venous

'Resectable'

- No distant metastases
- Clear fat plane around celiac, hepatic and superior mesenteric arteries
- No abutment of superior mesenteric vein or portal vein
‘Borderline Resectable’

- No distant metastases
- SMV/PV
  - Tumor abutment with impingement and narrowing of the lumen
  - Encasement or thrombus with proximal and distal vein segment that allows for reconstruction
- SMA
  - Abutment only

‘Locally Advanced’

- No distant metastases
- SMV/PV
  - Encasement
- SMA
  - Encasement
Recommendations:
1. Work up
   - CT (triple Phase), EUS, CXR, CA19-9
2. Functional Status assessment
3. Discussion of Goals of Treatment
4. Multi-Disciplinary Team Discussion
5. Consideration of Clinical Trial
6. Meet Criteria for Surgery First Approach

Criteria for Surgery First Approach
- No metastatic Disease
- Functional status appropriate for major surgery
- No evidence of tumor involvement in major vessels
- Ca19-9 supportive of potentially curative disease
  - (generally less than 1000)
Complications prevent chemotherapy and decrease survival

The Impact of Postoperative Complications on the Administration of Adjuvant Therapy Following Pancreat icoduodenectomy for Adenocarcinoma

- Only 54% of patients undergoing Open Whipple at the Johns Hopkins Hospital receive adjuvant chemotherapy
SURGICAL COMPLICATIONS DECREASE SURVIVAL

![Graph showing survival rates with different treatment sequences.](image)

Tzeng et al. ASO 2013

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**Improving Survival from Pancreas Cancer 2018**

- Change sequence of treatment
  - Earlier integration of new regimens

- Make surgery less morbid
  - More patients receive adjuvant therapy
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How do Surgeons decide which operation

Area Removed for Whipple  Area Removed for Distal Pancreatectomy

Types Pancreaticoduodenectomy

- Classic vs. Pylorus Preserving
- Extended Pancreaticoduodenectomy

Pancreaticoduodenectomy (Whipple)
Pylorus Preserving versus Classic

Cameron, JL. Surg Rounds 77-87, 1988

Extended PD with vascular resection

Technical risk factors for portal vein reconstruction thrombosis in pancreatic resection

http://dx.doi.org/10.1016/j.jvs.2015.01.061
**Extended Pancreaticoduodenectomy**

- More than half the stomach
- Colon resection
- Small bowel beyond first portion of the jejunum
- Vascular resection
- Kidney
- Liver
- diaphragm

**Distal Pancreatectomy**

Distal Pancreatectomy with En Bloc Celiac Axis Resection for Locally Advanced Pancreatic Adenocarcinoma Following Neoadjuvant Therapy

Joel M. Baumgartner · Alyssa Krausnikas · Mustapha Daouadi · Amer Zureikat · Wallis Marsh · Kenneth Lee · David Bartlett · A. James Moser · Herbert J. Zeh III
Central Pancreatectomy

Robotic-Assisted Minimally Invasive Central Pancreatectomy: Technique and Outcomes

Gerard J. Abood · M. Fatih Can · Mustapha Daouadi · Harold T. Huss · Jennifer Y. Steve · Lekshmi Ramalingam · Michael Stang · David L. Bartlett · Herbert J. Zeh III · A. James Moser

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MIS has potential to decrease morbidity

Evolution of surgical instruments

Optimizing Human abilities with Instruments

Augment Human skills with a Computer
Robotic platform is really computer assisted instrument

Computer Assisted Enhances Human Abilities
Computer makes all surgeons ambidextrous

Computer smooths motions and magnifies
Promise of Computer Assisted Pancreatic Surgery

- Improved Surgical Skills will lead to better outcomes for the patients
  - Decreased length of stay
  - Decreased morbidity
  - Faster return to baseline health and chemotherapy
  - Improved survival
This is just the beginning of skill enhancement

MIS Distal Pancreatectomy Standard

**Randomized Controlled Trial**

Minimally Invasive Versus Open Distal Pancreatectomy (LEOPARD)

A Multicenter Patient-blinded Randomized Controlled Trial

Thijs de Reuji, MD,* Erze van Blerk, MD,* Pieter van den Boscom, MD, PhD,† Peter van den Broeck, MD, PhD,‡ Freek Dassen, MD, PhD,* Ronald van Ens, MD, PhD,‡ Cres Dejongh, MD, PhD,‡ Emile van Dijk, MD, PhD,* Marcel Dikkers, PhD,‡

*Cooper van Eijk, MD, PhD,‡ Sebastian Felsen, MD, PhD,‡ Michael Gerards, MD, PhD,‡ Guus Geraedts, MD, PhD,‡‚‚‚ Guus Kusters, MD, PhD,‡‚‚‚ Gert-Jan van der Korst, MD, PhD,‡‚‚‚ Harm van der Meij, MD, PhD,‡‚‚‚ Harrie de Ryck, MD, PhD,‡‚‚‚ Misha Loyer, MD, PhD,‡‚‚‚ Gips Maas, MD, PhD,‡‚‚‚ Pascal Smedts, MD, PhD,‡‚‚‚ Marnix Smeets, MD, PhD,‡‚‚‚ and Mon Van Netveld, MD, PhD,‡,

†for the Dutch Pancreatic Cancer Group

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EQ-SD-3L: State of health visual analogue scale

QLQ-C30: Global health status

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Minimally invasive distal pancreatectomy. Open distal pancreatectomy.
6 Studies; 139 MIS compared to 343 Open

- EBL Favors MIS
- R0 Resection Favors MIS
- LN Harvest Favors MIS
- LOS Favors MIS

Robotic PD Associated with less complications

A Multi-institutional Comparison of Perioperative Outcomes of Robotic and Open Pancreaticoduodenectomy

Amer H. Zareikat, MD;1 Lauren M. Postlewait, MD;1 Yuan Liu, PhD;1 Therese W. Gillespie, PhD;1 Sharon M. Wolfe, MD;2 Daniel E. Abbott, MD;2 Syed A. Ahmad, MD;2 Shichuo K. Mathai, MD;2 Melisa E. Hogg, MD;2 Maken Zemaiti, MD, PhD, MPH;2 Clifford S. Cho, MD;1 Ahmed Salem, MD;1 Brent Xia, MD;3 Jennifer Steve, BS;3 Trang K. Nguyen, MD;3 Hari B. Keshava, MD;3 Sricharan Chakarova, MD;4 R. Matthew Walsh, MD;4 Mark S. Salamons, MD;5** Susan J. Storzer, LPN;5** David J. Benetrem, MD;5 Stephanie Lumpkin, MD;5 Hong J. Kim, MD;11 Herbert J. ZehIII, MD;11 and David A. Kooby, MD, FACS11

- MVA of 1200 Open and Robotic Whipples from 8 institutions.
- Robotic approach was associated with:
  - Increased operative time (75 min)
  - Reduction in operative blood loss
  - Reduction of major complications
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Surgery for locally advanced disease?

Radiological and Surgical Implications of Neoadjuvant Treatment With FOLFIRINOX for Locally Advanced and Borderline Resectable Pancreatic Cancer

Cristina R. Ferrone, MD, Giovanni Marchegiani, MD, Theodore S. Hong, MD, David P. Ryan, MD, Vikram Deshpande, MD, Erin L. McDonnell, Francesco Sebastiani, PhD, Daniela Dias Santos, MD, Jill N. Allen, MD, Lawrence S. Blazzuck, MD, Jeffrey W. Charn, MD, Jason E. Forst, MD, Lipika Goyal, MD, Eunice L. Koek, PhD, Janet K. Murphy, MD, David T. Tang, MD, Jennifer Y. Wo, MD, Andrew X. Zhu, PhD, Andrew L. Warshaw, MD, Keith D. Lillemoe, MD, and Carlos Fernandez-del Castillo, MD

The CT scan often does not change even with effective treatment
Surgery for locally advanced disease?

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Call to schedule an appointment

Harold C. Simmons Comprehensive Cancer Center

214-645-4673
UTswmed.org

Herbert.Zeh@UTsouthwestern.edu

Thank you for your participation.

If you have questions, please contact Patient Central at 877-2-PANCAN or e-mail patientcentral@pancan.org.

www.pancan.org