Pancreatic Cancer – Recent Progress

Richard D. Schulick, MD, MBA, FACS
Professor and Chair of Surgery
Mountain States Cancer Conference
November 5, 2016

Colorectal Cancer Metastases to Liver

Disclosures

Co-inventor of patent to use genetically modified Listeria monocytogenes to generate inflammatory response to cancer
Licensed to Aduro Biotech
Managed by Johns Hopkins University
Board of Noile Immune
Not compensated
Consultant to grandrounds.com
Provide remote second opinions for surgical oncology cases

Pancreatic Cancer Incidence and Death in USA 2016

Figure 1. Trends in Age-adjusted Cancer Death Rates by Site, Rates, US, 1930-2012

USA
Incidence: 53,000
Deaths: 42,000
Colorectal Cancer Metastases to Liver

Distal Pancreatectomy for Body and Tail Cancer

Pancreaticoduodenectomy for Head and Uncinate Cancer

Historical Perspective

1898
William S. Halsted
1st Chair of Surgery at Johns Hopkins
1st successful resection of ampullary cancer in jaundiced patient
Transduodenal local resection
Reanastamosed pancreatic and bile ducts to duodenum
Patient redeveloped jaundice 3 months later requiring reoperation and choledochojejunostomy
Patient died 6 months later of recurrence

Halsted, Boston Med Surg J. 1898
Colorectal Cancer Metastases to Liver

**Historical Perspective**

1909
Walter Kausch
Professor of Surgery of Victoria Hospital in Berlin
First successful 2-stage en bloc resection of head of pancreas and duodenum
Patient presented with obstructive jaundice from ampullary cancer
1st stage – cholecystojejunostomy and side-to-side enterolenterostomy
2nd stage – resection of head of pancreas, pylorus, and 1st and 2nd portions of duodenum
Reconstructed with gastrolenterostomy, closure of common bile duct, and anastomosis of pancreatic remnant to 3rd portion of duodenum
Patient died 9 months later of cholangitis without visible tumor at autopsy

Kausch, Zentralbl Chir. 1909

1935
Allen O. Whipple
Professor and Director of Surgery Presbyterian Hospital, New York (1921 – 1946)
Clinical Director Memorial Hospital, New York (1946 – 1951)
Reported 3 patients with ampullary cancer managed by 2-stage pancreaticoduodenectomy
3 patients survived 30 hours, 8 months, and 25 months

Whipple, Ann Surg. 1935

Colorectal Cancer Metastases to Liver

**Historical Perspective**

Two-stage procedure reported in 1935
One-stage procedure reported in 1942

Whipple, Ann Surg. 1935
Whipple, Rev Surg. 1963
Historical Perspective

Pancreaticoduodenectomy during the 1940’s – 1970’s

Many centers reported:
Operative mortalities 20 – 40 %
Postoperative morbidities 40 – 60 %

Pancreaticoduodenectomy during the 1980’s – present

Many centers reporting operative mortalities 1 – 2 %
Postoperative morbidities remain high 30 – 50%

John Cameron MD
Murray Brennan MD

Pancreaticoduodenectomies Performed at Johns Hopkins per Year

Survival - Pancreaticoduodenectomy for Ductal Adenocarcinoma per Decade

Winter, JoGS, 2006
Health Services Cost Review Commission (HSCRC)
Data in the State of Maryland from 1995-2004
Hospital Discharges for State of Maryland after Pancreatoduodenectomy
Data collected:
- Number of PD’s performed
- Presurgical morbid condition of patients
- Postoperative mortality
- Postoperative morbidity

Importance of Hospital Volume in Management of Pancreas Cancer

hospital volume/year

Mortality (n=2939)

Alive
Dead

Alive
Dead

Hospital volume/year

p < 0.001

(38 Hosp)
(2 Hosp)
(1 Hosp)

Importance of Hospital Volume in Management of Pancreas Cancer

Hospital Charges per Case (n = 2939)

$44,533
$79,622
$33,158

hospital volume/year

p < 0.001
What Needs to be Accomplished in the Next Decade?

**Impact on Survival**
Better understanding of molecular events and impaired pathways leading to disease
Prevention
Earlier detection
More effective systemic therapies
Multidisciplinary care of patients

**Impact on Quality of Life and Morbidity of Surgery**
Proper use of laparoscopic pancreatectomy

Better Understanding of Molecular Events and Impaired Pathways Leading to Disease

Model of Progression from Normal Cell to Metastatic Pancreatic Cancer

![Model of Progression](image-url)
Core Signaling Pathways in Human Pancreatic Cancers Revealed by Global Genomic Analyses (n=24)

24 patients
20,661 genes analyzed by sequencing
1327 had at least one mutation
148 had two or more mutations
High number of alterations per cancer/patient

Majority of pancreatic cancers have genetic alterations in 12 partially overlapping processes
Pathway components that are altered in any individual tumor vary widely
Unlike other neoplasms, driven by a single targetable oncogene, pancreatic cancer result from alterations of a large number of pathways and processes
Best hope for therapeutics will be in discovery of agents that target physiologic effects of altered pathways and processes rather than individual genes

Whole genomes redefine the mutational landscape of pancreatic cancer
Prevention of Pancreatic Cancer

<table>
<thead>
<tr>
<th>Risk Factor</th>
<th>Odds Ratio</th>
<th>95% CI</th>
</tr>
</thead>
<tbody>
<tr>
<td>Former Smoker</td>
<td>1.29</td>
<td>1.07 - 1.54</td>
</tr>
<tr>
<td>Current Smoker</td>
<td>3.40</td>
<td>2.28 - 5.07</td>
</tr>
<tr>
<td>Diabetes</td>
<td>2.54</td>
<td>1.87 - 3.46</td>
</tr>
<tr>
<td>Long-standing Diabetes</td>
<td>3.09</td>
<td>2.02 - 4.72</td>
</tr>
<tr>
<td>Diabetes and Current Smoker</td>
<td>4.79</td>
<td>3.00 - 7.65</td>
</tr>
<tr>
<td>Long-standing Diabetes and Current Smoker</td>
<td>6.03</td>
<td>3.41 - 10.85</td>
</tr>
</tbody>
</table>

Earlier Detection:
Patients with Premalignant Cysts
Patients in High Risk Families
Colorectal Cancer Metastases to Liver

Earlier Detection

Blood test captures rare cancer cells

A sensitive blood test that can detect a single cancer cell out of a billion healthy ones has the potential to transform cancer treatment. It is closer to becoming available at doctor offices.

The process of capturing cancer cells:

A microchip the size of a business card is used and is covered in 75,000 tiny pores. Cancer cells stick and then are covered with antibodies that attract cancer cells.

Prevalence of Unsuspected Pancreatic Cysts (CT)

<table>
<thead>
<tr>
<th>Parameter</th>
<th>Patients Screened (% of total)</th>
<th>Patients with Cyst/Prevalence per 100 (95% CI)</th>
<th>Odds Ratio* (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Total</td>
<td>2,052 (100)</td>
<td>73</td>
<td>2.6 (2.0–3.3)</td>
</tr>
<tr>
<td>Age (y)</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>20–29</td>
<td>282 (13.7)</td>
<td>0</td>
<td>0</td>
</tr>
<tr>
<td>30–49</td>
<td>711 (34.8)</td>
<td>11</td>
<td>1.5 (0.6–3.9)</td>
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<tr>
<td>50–59</td>
<td>426 (21.1)</td>
<td>10</td>
<td>2.9 (1.5–5.3)</td>
</tr>
<tr>
<td>60–69</td>
<td>350 (16.5)</td>
<td>22</td>
<td>4.6 (2.4–8.5)</td>
</tr>
<tr>
<td>≥ 70</td>
<td>183 (8.9)</td>
<td>16</td>
<td>8.7 (4.0–18.2)</td>
</tr>
<tr>
<td>Sex</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>F</td>
<td>1,507 (73.0)</td>
<td>35</td>
<td>2.5 (1.7–3.3)</td>
</tr>
<tr>
<td>M</td>
<td>1,445 (70.0)</td>
<td>38</td>
<td>2.6 (1.6–4.2)</td>
</tr>
</tbody>
</table>

Cystic Lesions of the Pancreas

- Intraductal Papillary Mucinous Neoplasm
- Mucinous Cystic Neoplasm
- Serous Cystadenoma
- Solid and Pseudo-Papillary Neoplasm
- Lymphoepithelial Cyst
- Cystic Neuroendocrine Tumor

Cunningham, Schulick, WJG Surg, 2010
Colorectal Cancer Metastases to Liver

IPMN - Introduction

Develops from pancreatic ductal epithelium:
- Mucin production
- Cystic dilatation of pancreatic duct
- Intraductal papillary growth

World Health Organization in 2000 classified these tumors as IPMN

IPMN further classified histologically:
- Adenoma (benign)
- Borderline (moderate dysplasia)
- Carcinoma in situ (high grade dysplasia)
- Malignant (carcinoma)

Sohn, Ann Surg, 2004

Colorectal Cancer Metastases to Liver

IPMN - Introduction

IPMN can further be classified by location

Main duct

Branch duct

Tanaka, Pancreatology, 2005
Tanaka, J Gastroent, 2005
Kawamoto, Radiographics, 2005

Colorectal Cancer Metastases to Liver

IPMN – Diagnostic Workup

Traditionally
- ERCP with classic triad:
  - Bulging ampulla of Vater
  - Mucin production
  - Dilated pancreatic duct

Presently
- Multi-slice CT scan
- EUS ± FNA

Other tests
- MRI/MRCP + secretin
- Pancreatic ductoscopy

Sohn, Ann Surg, 2004
Colorectal Cancer Metastases to Liver

Main Duct IPMN

Branch Duct IPMN

<table>
<thead>
<tr>
<th>Reference (Year)</th>
<th>Patients</th>
<th>Median Age (Yr)</th>
<th>Median size (cm)</th>
<th>X-ray/CT</th>
<th>Needle biopsy</th>
<th>Survival (OS, N)</th>
<th>Survival (RRS, N)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Main Duct IPMN</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Branch Duct IPMN</td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Tanaka, Pancreatology, 2006

Familial Pancreatic Cancer Metastases to Liver

Hereditary Pancreatic Cancer

Syndromes of Chronic Inflammation

<table>
<thead>
<tr>
<th>Reference</th>
<th>Clinical Features</th>
<th>Hereditary Markers</th>
<th>Endocrine Markers</th>
</tr>
</thead>
<tbody>
<tr>
<td>Familial Cancer</td>
<td>20-40</td>
<td>BRCA2, Brat, TSC1, TSC2, RH5</td>
<td></td>
</tr>
<tr>
<td>Menkes Syndrome</td>
<td>40-50</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Neurofibromatosis</td>
<td>50-60</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Marfan Syndrome</td>
<td>60-70</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

Templeton, Surg Clin N Am, 2013
More Effective Systemic Therapies: Adjuvant Therapy Immunotherapy

Adjuvant Therapy of Pancreatic Cancer

Adjuvant therapy for pancreas cancer has become standard of care (GITSG, EORTC, ESPAC-1, CONKO-001, ESPAC-3, RTOG 97-04)

- Single-agent gemcitabine
- 5FU/Leucovorin (S-1)

Unresolved questions
- Does chemoradiotherapy impact overall survival?
- Does addition of a second or third cytotoxic or biologic agent improves outcome when added to gemcitabine?
Colorectal Cancer Metastases to Liver

<table>
<thead>
<tr>
<th>Group</th>
<th>Patients</th>
<th>Trial Design</th>
<th>Primary Endpoint</th>
</tr>
</thead>
<tbody>
<tr>
<td>CRC004</td>
<td>1424</td>
<td>Gemcitabine vs gemcitabine</td>
<td>Overall survival</td>
</tr>
<tr>
<td>COMBO 065</td>
<td>412</td>
<td>Gemcitabine vs gemcitabine</td>
<td>Equivalent median 11.4 vs 11.0 months disease-free survival between groups reported (P = 0.11)</td>
</tr>
<tr>
<td>RTG 088 (PCTC156904)</td>
<td>852</td>
<td>First randomization: gemcitabine vs gemcitabine (low vs high), second randomization: gemcitabine vs gemcitabine (low vs high)</td>
<td>Overall survival</td>
</tr>
<tr>
<td>PDCDIAACCORD 24-098 (PCTC156904)</td>
<td>496</td>
<td>Gemcitabine vs FOLFOXIRI</td>
<td>Disease-free survival at 3 y</td>
</tr>
<tr>
<td>APCTG</td>
<td>808</td>
<td>Gemcitabine vs gemcitabine (low vs high)</td>
<td>Disease-free survival</td>
</tr>
<tr>
<td>NonLinke Genetics Corporation</td>
<td>722</td>
<td>Gemcitabine (i.e. chemotherapy) +/- Gemcitabine immunotherapy</td>
<td>Overall survival</td>
</tr>
</tbody>
</table>

Kobayashi, O'Reilly, Surg Onc Clin N Am, 2016

More Effective Systemic Therapies

Identification of CD112R as a novel checkpoint for human T cells

Yuma Zhao, Alexander M. Canedy, Melissa C. Bachok, Alastair A. M. Macintyre, Julie E. Flanagan, John T. Burns, Seong Y. Sim, Thomas D. Ham, and Beth H. East

CD112R blockade improves anticancer immunity in a lung metastasis mouse model

Targeting the CD112R pathway in the adaptive tumor response in mouse tumor model
The CD112R complex holds significant potential as a novel therapeutic target

- CD12 expression and CD112R binding confirmed in multiple cancer models
- Multiple reagents identified with encouraging initial data (mAB, CAR-T, Fusion Protein)
- Preparing additional in vivo data

Proof of Principle

Intellectual Property

- Unclaimable patent positions and methods
- World class know-how in cell surface signaling, immunology and cancer

Industrial Enthusiasms

- Big Pharma: Merck, GSK, ONO
- Startup and investors: Arcana, NextCure, TopoLife

The CD112R pathway is heavily expressed in human cancers

- Borderline Resectable Pancreatic Cancer

TH 64 yo Female – June 2012
Definition of Borderline Resectable Pancreatic Adenocarcinoma

Borderline Resectable

• No distant metastases
• Venous (SMV + PV)
  • Abutment (<180°)
  • Short segment encasement (>180°)
  • Short segment occlusion with suitable access for reconstruction
• Arterial (hepatic and superior mesenteric)
  • SMA: Abutment (≤180°) but not encasement (>180°)
  • HA: Short segment abutment (≤180°) or encasement (>180°)

Evans, Schulick, Ann Surg Onc, 2009

TH 64 yo Female – Oct 2012

TH 64 yo Female

Underwent pancreaticoduodenectomy with resection of portal, superior mesenteric, and splenic vein confluence. Portal and superior mesenteric vein reconstructed primarily with ligature of splenic vein
Path T3N1M0
2.8 cm adenocarcinoma
5/16 LN positive
Cancer did not infiltrate vein wall, but densely adherent
Margin negative
Patient survived 30 months and then died of metastatic disease
Colorectal Cancer Metastases to Liver

17/18 went to resection and R0

Overall Survival and R

Progression Free Survival

Overall Survival

Overall Survival and Cycles

Full dose neoadjuvant FOLFIRINOX is associated with prolonged survival in patients with locally advanced pancreatic adenocarcinoma.

Technical risk factors for portal vein reconstruction thrombosis in pancreatic resection:

- Long operative times and prosthetic grafts are risk factors
- Preferentially use primary, patch, vein interposition repair
Multidisciplinary Care of Pancreatic Cancer Patients

- Diagnosis
- Meet with Surgeon
- Meet with Chemotherapy Dr.
- Meet with Radiation Dr.
- Meet with Gastroenterologist
- Start Treatment

Weeks: 0, 1, 2, 3, 4, 5

Are they talking to each other?
Do they remember who the patient is?
Are they offering the best cutting edge therapies?

Better Model of Taking Care of Pancreatic Cancer Patients

- 8 AM: Review of previous patient visit
- 9 AM: Patient present
- 10 AM: History and Physical
- 11 AM: Oncology, Medical, Pathology, Genetics
- 12 PM: Review of previous patient visit

Physicians:
- Surgical Oncology
- Medical Oncology
- Radiation Oncology
- Pathology
- Genetics
- Anesthesiology (Pain, Symptology)

Physicians meet with patients, summarize plan for patients.
University of Colorado Hospital
Pancreatic and Biliary Multidisciplinary Clinic

Colorectal Cancer Metastases to Liver

Decreasing Surgical Impact on Quality of Life?
Laparoscopic Pancreatic Surgery

Minimally Invasive Surgery for the Pancreas

**Cons**
- Specialized Equipment
- Geologic Complications
- Technical Difficulty

**Pros**
- Decreased Blood Loss
- Fewer Wound Complications
- Faster Recovery
**Colorectal Cancer Metastases to Liver**

**Totally Laparoscopic Whipple Video**

**DISTRIBUTION OF CASES**

<table>
<thead>
<tr>
<th>TOTAL LAPAROSCOPIC WHIPPLE ATTEMPTED (Oct 2012 – August 2016)</th>
<th>TOTAL LAPAROSCOPIC WHIPPLE COMPLETED</th>
<th>CONVERTED TO OPEN</th>
</tr>
</thead>
<tbody>
<tr>
<td>70</td>
<td>66 (94.3%)</td>
<td>4 (5.7%)</td>
</tr>
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</table>

**DEMOGRAPHIC**

<table>
<thead>
<tr>
<th>VARIABLE</th>
<th>N(%).</th>
</tr>
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<tbody>
<tr>
<td>AGE (median, range)</td>
<td>66.1 (55 – 72).</td>
</tr>
<tr>
<td>GENDER</td>
<td></td>
</tr>
<tr>
<td>Male</td>
<td>31 (44.3%).</td>
</tr>
<tr>
<td>BMI (median, range)</td>
<td>25.4 (22.2 – 28.5).</td>
</tr>
<tr>
<td>SMOKING STATUS</td>
<td></td>
</tr>
<tr>
<td>Never</td>
<td>32 (45.7%).</td>
</tr>
<tr>
<td>Former</td>
<td>28 (40.0%).</td>
</tr>
<tr>
<td>Current</td>
<td>10 (14.3%).</td>
</tr>
<tr>
<td>COMORBIDITIES</td>
<td></td>
</tr>
<tr>
<td>COPD</td>
<td>13 (18.6%).</td>
</tr>
<tr>
<td>HTN</td>
<td>42 (45.7%).</td>
</tr>
<tr>
<td>Diabetes</td>
<td>11 (15.7%).</td>
</tr>
<tr>
<td>MI</td>
<td>2 (2.9%).</td>
</tr>
<tr>
<td>CKD</td>
<td>6 (8.6%).</td>
</tr>
<tr>
<td>DVT/PE</td>
<td>5 (7.1%).</td>
</tr>
<tr>
<td>ASA CLASS</td>
<td></td>
</tr>
<tr>
<td>I</td>
<td>3 (4.5%).</td>
</tr>
<tr>
<td>II</td>
<td>57 (81.1%).</td>
</tr>
<tr>
<td>III</td>
<td>7 (10.1%).</td>
</tr>
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### Prior Surgeries

<table>
<thead>
<tr>
<th>Variable</th>
<th>N (%), n (%)</th>
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<tbody>
<tr>
<td>Appendectomy</td>
<td>10 (14.3%)</td>
</tr>
<tr>
<td>Cholecystectomy</td>
<td>12 (17.1%)</td>
</tr>
<tr>
<td>Ventral Hernia</td>
<td>3 (4.3%)</td>
</tr>
<tr>
<td>TAH &amp; BSO</td>
<td>12 (17.1%)</td>
</tr>
<tr>
<td>Gastric Resection</td>
<td>1 (1.4%)</td>
</tr>
<tr>
<td>Small Bowel Resection</td>
<td>1 (1.4%)</td>
</tr>
<tr>
<td>Large Bowel Resection</td>
<td>1 (1.4%)</td>
</tr>
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### Operative & Perioperative Characteristics

<table>
<thead>
<tr>
<th>Variable</th>
<th>N (%), n (%)</th>
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</thead>
<tbody>
<tr>
<td>Operative Time (min)</td>
<td>Median (range), Mean (SD)</td>
</tr>
<tr>
<td></td>
<td>335.5 (298–377), 345.2 (±66.6)</td>
</tr>
<tr>
<td>Estimated Blood Loss (ml)</td>
<td>Median (range), Mean (SD)</td>
</tr>
<tr>
<td></td>
<td>300 (150–450), 334.2 (±264.2)</td>
</tr>
<tr>
<td>Tumor Size (cm, max diameter)</td>
<td>Median (range), Mean (SD)</td>
</tr>
<tr>
<td></td>
<td>2.1 (1.3–3.2), 2.3 (±1.4)</td>
</tr>
<tr>
<td>Surgical Margins</td>
<td>Negative (R0)</td>
</tr>
<tr>
<td></td>
<td>63 (95.5%)</td>
</tr>
<tr>
<td>Number of Nodes Harvested</td>
<td>Median (range), Mean (SD)</td>
</tr>
<tr>
<td></td>
<td>18.5 (15.0–22.0), 18.8 (±7.4)</td>
</tr>
<tr>
<td>Epidural</td>
<td>4 (6.1%)</td>
</tr>
<tr>
<td>ICU LOS (days)</td>
<td>Median (range), Mean (SD)</td>
</tr>
<tr>
<td></td>
<td>1 (1–1), 1.5 (±1.3)</td>
</tr>
<tr>
<td>ICU Readmission</td>
<td>10 (15.2%)</td>
</tr>
<tr>
<td>Hospital LOS (days)</td>
<td>Median (range), Mean (SD)</td>
</tr>
<tr>
<td></td>
<td>10.5 (8–14), 13.5 (±11.1)</td>
</tr>
<tr>
<td>Readmission (90 days)</td>
<td>16 (24.2%)</td>
</tr>
<tr>
<td>Death (30 days)</td>
<td>0</td>
</tr>
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### COMPLICATIONS

<table>
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<tr>
<th>Variable</th>
<th>N (%)</th>
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<tbody>
<tr>
<td>Pancreatic fistula</td>
<td>35 (53.0%)</td>
</tr>
<tr>
<td>Grade A</td>
<td>19 (28.8%)</td>
</tr>
<tr>
<td>Grade B</td>
<td>13 (21.7%)</td>
</tr>
<tr>
<td>Grade C</td>
<td>3 (5.0%)</td>
</tr>
<tr>
<td>Delayed gastric emptying</td>
<td></td>
</tr>
<tr>
<td>Grade A</td>
<td>5 (7.6%)</td>
</tr>
<tr>
<td>Grade B</td>
<td>5 (7.6%)</td>
</tr>
<tr>
<td>Grade C</td>
<td>2 (3.0%)</td>
</tr>
<tr>
<td>Bile leak</td>
<td>4 (6.1%)</td>
</tr>
<tr>
<td>Pseudoaneurism GDA</td>
<td>2 (3.0%)</td>
</tr>
<tr>
<td>Pancreatic artery dilation</td>
<td>1 (1.5%)</td>
</tr>
<tr>
<td>Chyle leak</td>
<td>3 (4.6%)</td>
</tr>
<tr>
<td>Surgical site infection</td>
<td>5 (7.6%)</td>
</tr>
<tr>
<td>Marginal ulcer</td>
<td></td>
</tr>
<tr>
<td>Intrabdominal bleeding</td>
<td>13 (19.7%)</td>
</tr>
<tr>
<td>Incisional hernia</td>
<td>2 (3.0%)</td>
</tr>
<tr>
<td>Postoperative transfusion</td>
<td>11 (16.7%)</td>
</tr>
</tbody>
</table>

### INTERVENTION

<table>
<thead>
<tr>
<th>Category</th>
<th>N (%)</th>
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<tbody>
<tr>
<td>Coil embolization</td>
<td>8 (12.1%)</td>
</tr>
<tr>
<td>PTC</td>
<td>8 (12.1%)</td>
</tr>
<tr>
<td>Percutaneous drain</td>
<td>17 (25.8%)</td>
</tr>
<tr>
<td>Gastrojejunal dilation</td>
<td>1 (1.5%)</td>
</tr>
<tr>
<td>Transfusion</td>
<td>11 (16.7%)</td>
</tr>
</tbody>
</table>

### TUMOR RELATED OUTCOME

<table>
<thead>
<tr>
<th>Variable</th>
<th>N (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>FOLLOW UP (months)</td>
<td></td>
</tr>
<tr>
<td>Median (range)</td>
<td>6.0 (2.0 - 11.5)</td>
</tr>
<tr>
<td>Mean (sd)</td>
<td>8.1 (+7.9)</td>
</tr>
<tr>
<td>RECURRENCE</td>
<td></td>
</tr>
<tr>
<td>Extent</td>
<td>7 (10.6%)</td>
</tr>
<tr>
<td>Liver regional</td>
<td>6 (9.1%)</td>
</tr>
</tbody>
</table>
Pathology of Resected Lesions
Total Laparoscopic Pancreaticoduodenectomy

Operative Time (minutes)

Patients in chronological order

Estimated Blood Loss (mL)

Patients in chronological order
Pancreatic cancer is a deadly disease. Pancreatectomy can be performed with low mortality, but still with high complications rates. Best results are accomplished at high volume centers.

To Impact on Survival:
- Better understanding of molecular events and impaired pathways leading to disease
- Prevention
- Earlier detection
- More effective systemic therapies
- Multidisciplinary care of patients

To impact on Quality of Life and Morbidity of Surgery:
- Proper use of laparoscopic pancreatectomy
- (Decrease pancreatic fistula rate)