COLLECTING CANCER DATA: PANCREAS

Q&A

• Please submit all questions concerning webinar content through the Q&A panel.
• Reminder:
• If you have participants watching this webinar at your site, please collect their names and emails.
• We will be distributing a Q&A document in about one week. This document will fully answer questions asked during the webinar and will contain any corrections that we may discover after the webinar.
AGENDA

- Overview
  - Anatomy
  - Histology
  - Epi moment
- Quiz 1
- Stage
- Treatment
- Quiz 2
- Case Scenarios
OVERVIEW
ANATOMY AND FUNCTION
ROLES OF THE PANCREAS

- Exocrine
  - Aids in digestion
  - Secretion of enzymes

- Endocrine
  - Blood sugar control & metabolism
  - Secretion of insulin & other hormones
**ENDOCRINE FUNCTION OF THE PANCREAS**

- Blood Sugar Regulation & Metabolism

**REGIONAL LYMPH NODES**

- Superior mesenteric
- Anterior and posterior pancreaticoduodenal
- Pyloric
- Proximal mesenteric
- Common bile duct lymph nodes
- Splenic hilar, pancreatic tail, peripancreatic, hepatic artery, retroperitoneal, lateral aortic
- Head only
  - Infrapyloric, subpyloric, celiac
- Body & Tail only
  - pancreaticocolienal, splenic
DISTANT METASTASIS

- Liver
- Peritoneal Cavity
- Lungs

HISTOLOGY
IMPORTANT REMINDER

Please check the 2018 ICD-O-3 Update Table first to determine if the histology is listed. If the histology is not included in the update, then review the ICD-O-3 and/or Hematopoietic and Lymphoid Database and/or Solid Tumor (MP/H) rules.

NEW HISTOLOGIES WITH PANCREAS

New Term (C25._)

- 8453/3 Intraductal papillary mucinous neoplasm (IPMN) with an associated invasive carcinoma
- 8453/2 Intraductal papillary mucinous neoplasm with high-grade dysplasia
- 8503/2 Intraductal tubulopapillary neoplasm
- 8470/3 Mucinous cystic tumor with associated invasive carcinoma
EXAMPLE

- Final Diagnosis: biopsy, body of pancreas, mixed acinar ductal carcinoma

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<th>2018 Histology</th>
<th>2017 Histology</th>
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<td>Mixed acinar ductal carcinoma</td>
<td>Y</td>
<td>Cases diagnosed prior to 1/1/2018 use code 8523/3</td>
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POP QUIZ

- Final Diagnosis: Ductal carcinoma of the pancreas

<table>
<thead>
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<th>Primary Site</th>
<th>2018 Histology</th>
<th>2017 Histology</th>
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</thead>
<tbody>
<tr>
<td>C25.9</td>
<td>8500/3</td>
<td>8500/3</td>
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</table>
QUESTIONS?

EPI MOMENT...
THEME SONG: TRUCKIN’
DESCRIPTIVE EPIDEMIOLOGY

- Analyzed alone; tobacco-associated (C25.1)
- Incidence 10th
  - 14.5 per 100,000 men; ↑ 1%
  - 11.2 women; ↑ 1.1%
  - 17.0 black men; ↑ .6%
  - 14.6 black women; ↑ 0.8%
- Mortality 4th:
  - 12.6 per 100,000 men; ↑ 0.2%
  - 9.5 women; ↑ 0.2%
  - 14.8 black men; ↓ 0.5%
  - 12.2 black women; ↓ 0.2%
- I/M Ratio >1.0

INCOMPETENCE & MORTALITY: US
ETIOLOGY/RISK FACTORS

• Most cases are sporadic
• KRAS mutation ≈85-95%
• Heredity: 2+ family (6x), BRCA2 (3.5x), PRSS1, STK11, CDKN2A, CTFR, MLH1, APC
• Chronic pancreatitis, smoking (2x), obesity (2x)
• Diabetes: Diabetes dx often temporally close (reverse causation)
• Occupational chemical exposures
• Infectious (*H pylori, HBV*)?
• NO RISK: alcohol, coffee or radiation

HISTOLOGY

• Exocrine
  • Ductal adenocarcinoma
    • >90% of all pancreatic cancers
    • 75% in head of pancreas
  • Cystic <1%
• Endocrine
  • Islet-cell/neuroendocrine are rare
PROGRESSION: PanIN TO INVASIVE DUCTAL ADENOCARCINOMA

SCREENING
- Population-based
  - none
- High-risk
  - Experimental
  - Mutations (Kras, p53, p16)
  - Protein patterns
  - Blood marker (CA19-9—but generally as guide for disease progression)
  - MiRNA
SIGNS & SYMPTOMS

- Average age at dx: 71
  - Generally asymptomatic until late stage
- Jaundice
- Abdominal pain and/or lower back pain
- Rapid weight loss
- Bloating
- Loss of appetite and/or nausea
- Discolored stool
- Dermatitis
- Diabetes

TESTS

- PE: palpable mass
- CT, Ultrasound
- MRCP: magnetic resonance cholangiopancreatography
- ERCP: endoscopic retrograde cholangiopancreatography
- Blood tests: amylase & lipase
- Biopsy: surgical or needle
PATRICK SWAYZE VERSUS STEVE JOBS

- Disease of same name but not the same
- Jobs—neuroendocrine/islet cell
  - Rarer, slower growing, easier to treat
  - 8 years; age 56; non-smoking vegan
- Swayze—ductal adenocarcinoma
  - Median survival 5 months
  - 20 months; age 57; active but smoker
  - Gemcitabine
SUMMARY STAGE
PANCREAS

SUMMARY STAGE 2000

Pancreas: head, body, and tail
• C25.0 Head of pancreas
• C25.1 Body of pancreas
• C25.2 Tail of pancreas
• C25.3 Pancreatic duct
• C25.4 Islets of Langerhans

Pancreas: other and unspecified
• C25.7 Other and unspecified parts of pancreas (neck)
• C25.8 Overlapping lesion of pancreas
• C25.9 Pancreas, NOS

SUMMARY STAGE 2018

- Pancreas (including NET Pancreas)
  - C250 Head of pancreas
  - C251 Body of pancreas
  - C252 Tail of pancreas
  - C253 Pancreatic duct
  - C254 Islets of Langerhans
  - C257 Other specified parts of pancreas
  - C258 Overlapping lesion of pancreas
  - C259 Pancreas, NOS

https://staging.seer.cancer.gov/eod_public/list/1.0/

POP QUIZ

- Ultrasound: 6 cm mass located in the tail of the pancreas. The tumor directly invades the spleen with adenopathy of splenic nodes, most likely malignant. No liver metastasis.
- Biopsy of pancreatic tail mass: Adenocarcinoma

- Summary Stage 2000 4-Regional by BOTH direct extension AND regional lymph node(s) involved
- Summary Stage 2018
AJCC STAGING

CHAPTER 28: EXOCRINE PANCREAS PAGE 337
CHAPTER 34: NEUROENDOCRINE TUMORS OF THE PanCREAS PAGE 407

AJCC 8TH EDITION ERRATA

• Chapter 28-Exocrine Pancreas
  • No Errata
• Chapter 34-Neuroendocrine Tumors of the Pancreas
  • T3: Tumor limited to the pancreas,* >4 cm; or tumor invading the duodenum or common bile duct
SITE/HISTOLOGIES ELIGIBLE FOR STAGING

• A site and histology combination must be assigned a Disease Number (AJCC ID) to be assigned an AJCC Stage.

https://cancerstaging.org/references-tools/deskreferences/Pages/8EUpdates.aspx

POP QUIZ 1

• A registrar is abstracting a 2018 pancreas primary. She has entered primary site code of C25.0 and the histology is 8070/3.

• When she gets to the TNM Fields she gets a message that the case is not eligible for an AJCC Stage.

• Is this correct?

• What if the physician assigned an AJCC Stage?
CHAPTER 28 EXOCRINE PANCREAS

SUMMARY OF CHANGES

- Reclassification of the T values
- Reclassification of the N values
NEUROENDOCRINE CARCINOMA

- Chapter 34-Neuroendocrine Tumors Pancreas
  - Neuroendocrine Tumor, well differentiated (8240/3)
  - Neuroendocrine Tumor, moderately differentiated (8249/3)
- Chapter 28-Exocrine Pancreas
  - Neuroendocrine Tumor, NOS (8246/3)
  - Neuroendocrine Tumor, poorly differentiated (8246/3)

RULES FOR CLASSIFICATION

- General Rules
- Clinical
  - Must have a diagnosis of cancer
  - Must have some kind of work-up
- Pathological
  - Resection of the primary tumor or
  - Pathologic confirmation of distant mets
CLINICAL WORK-UP

- Imaging
- Endoscopic ultrasound and fine needle aspiration
- Staging laparoscopy
- ERCP

POP QUIZ 2

- Imaging shows a 3.2cm malignant appearing tumor in the body of pancreas.
  - The tumor encases the superior mesenteric artery.
  - No enlarged lymph nodes or metastasis identified.
  - An exploratory laparotomy showed metastatic nodules on the surface of the liver.
  - A biopsy of a metastatic nodule showed metastatic ductal carcinoma.

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<td>Stage</td>
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<tr>
<td>Stage</td>
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PREOPERATIVE NEOADJUVANT TREATMENT

- Borderline resectable
- Resectable

PATHOLOGIC STAGING

- Resection of the primary tumor and regional nodes required if patient does not have pathologic confirmation of distant mets.
ASSIGNING VALUES

- T value
  - Non-invasive
  - Invasive tumor: based on tumor size
- N value is based on number of positive lymph nodes
- M value is absence or presence of distant mets
- Stage group is based on T,N, and M only

POP QUIZ 3

- Imaging shows a 1.7 cm tumor in the tail of pancreas.
  - The tumor abuts the superior mesenteric artery. There is less than 180° of involvement. No additional arterial or celiac axis involvement.
  - No enlarged lymph nodes or metastasis identified.
  - An EUS-FNA confirms poorly differentiated acinar carcinoma
- The patient is treated with neoadjuvant chemoradiation.

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<tr>
<td>Stage</td>
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POP QUIZ 3 (CONT)

- The patient went on to have a distal pancreatectomy.
- Pathology did not show any residual tumor.
- 17 lymph nodes were resected. No malignancy was identified.

Pathological Stage group is blank!

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SITE SPECIFIC DATA ITEMS/GRADE

- No SSDI’s related to pancreas
- Standard Grade data items

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<th>Description</th>
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<tr>
<td>1</td>
<td>G1: Well differentiated</td>
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<tr>
<td>2</td>
<td>G2: Moderately differentiated</td>
</tr>
<tr>
<td>3</td>
<td>G3: Poorly differentiated</td>
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<tr>
<td>9</td>
<td>Grade cannot be assessed (GX); Unknown</td>
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GRADE

• A patient is found to have a tumor in the pancreas.
  • A biopsy confirms poorly differentiated mucinous carcinoma.
  • The patient had neoadjuvant treatment followed by a whipple procedure.
  • Pathology shows a moderately differentiated mucinous carcinoma.

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<td>Pathological Grade</td>
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<tr>
<td>Post-therapy Grade</td>
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QUESTIONS?
SUMMARY OF CHANGES

- New Chapter (previously included with exocrine/endocrine chapters)
- No Tis
- Subdivision of the M category
RULES FOR CLASSIFICATION

• General Rules
• Clinical
  • Must have a diagnosis of cancer
  • Must have some kind of work-up
• Pathological
  • Resection of the primary tumor or
  • Pathologic confirmation of distant mets

CLINICAL WORK-UP

• Imaging
• Endoscopic ultrasound and fine needle aspiration
• Staging laparoscopy
• ERCP
PATHOLOGIC STAGING

- Resection of the primary tumor and regional nodes required if patient does not have pathologic confirmation of distant mets.

ASSIGNING VALUES

- T value
  - Tumor size
  - Invasion of duodenum or common bile duct
  - Invasion of adjacent organs or vessels
- N value is based on number of positive lymph nodes
- M value is absence or presence of distant mets and where metastasis occurs
- Stage group is based on T, N, and M only
POP QUIZ 4

- A patient had a CT that showed a 6.5cm tumor in the tail of the pancreas that invaded into the duodenum. Several hypervascular lesions suspicious for metastasis were seen in the liver.
- An EUS-FNA of the pancreatic tumor revealed a well differentiated neuroendocrine carcinoma.

### Data Item 8th ed

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<tr>
<td>Stage</td>
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</table>

POP QUIZ 4 (cont)

- The surgeon performed a distal pancreatectomy with splenectomy combined with left lateral hepatectomy and intraoperative radiofrequency ablation of 2 tumors in the right lobe.
- Pathologic analysis confirmed metastatic well-differentiated pancreatic NET with 2 mitoses per 10 high-powered fields.
  - Tumor size: 6.5cm
  - Extension: There was invasion into, but not through the duodenum wall.
  - 4 of 22 common hepatic lymph nodes were positive for metastasis.

### Data Item 8th ed

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SITE SPECIFIC DATA ITEMS/GRADE

- Grade

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<th>Description</th>
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<tr>
<td>1</td>
<td>G1: Mitotic count (per 10 HPF) less than 2 AND Ki-67 index (%) less than 3</td>
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<tr>
<td>2</td>
<td>G2: Mitotic count (per 10 HPF) equal 2-20 OR Ki-67 index (%) equal 3-20</td>
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<tr>
<td>3</td>
<td>G3: Mitotic count (per 10 HPF) greater than 20 OR Ki-67 index (%) greater than 20</td>
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<tr>
<td>A</td>
<td>Well differentiated</td>
</tr>
<tr>
<td>B</td>
<td>Moderately differentiated</td>
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<tr>
<td>C</td>
<td>Poorly differentiated</td>
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<tr>
<td>D</td>
<td>Undifferentiated, anaplastic</td>
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<tr>
<td>9</td>
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POP QUIZ 5

- An EUS-FNA of the pancreatic tumor revealed a well differentiated neuroendocrine carcinoma.
- Pathologic analysis confirmed metastatic well-differentiated pancreatic NET with 2 mitoses per 10 high-powered fields. Ki-67 was 14%
QUESTIONS?

TREATMENT
TREATMENT

• Poor survival rate with any stage of pancreatic exocrine cancer
• Pain control important part of treatment
• Clinical trials
  • Appropriate treatment alternatives for patients with any stage of disease

TREATMENT

• Surgical resection is only potentially curative technique
  • More than 80% of patients present with disease that cannot be cured with resection
  • Median survival of resected patients ranges from 15-19 months
• Ablation/emobolization
• Radiation
• Chemo & other drugs
SURGICAL STATUS

• Resectable
  • Tumor within or limited extension beyond pancreas
  • Patient is healthy (major operation)
  • Based on the high probability of obtaining negative resection margins (R0)—using imagery
• Borderline resectable
  • Reached but not deep/surrounding blood vessels
  • Neoadjuvant chemo (sometimes w/radiation) often first or followed
• Unresectable
  • Surgery palliative
  • Chemo often followed by chemoradiation (but higher risk of side effects)

CRITERIA FOR RESECTION

• No peritoneal or hepatic metastasis
• No abutment, distortion, thrombus, or venous encasement of the portal or superior mesenteric vein
• Must have a clear fat plane around the celiac axis, hepatic artery, and superior mesenteric vein
• Surgery may determine not resectable
  • Surgery stopped or modified to palliative
WORK-UP

• Pancreatic protocol CT
• Pancreas protocol MRI
• Endoscopic ultrasound (EUS)
• Endoscopic retrograde cholangiopancreatography (ERCP)
• Biopsy
  • CT guided
  • EUS guided (preferred)

SURGERY

• Pancreatoduodenectomy (Whipple procedure)
  • Removal of:
    • Distal half of the stomach (antrectomy)
    • Gall bladder and its cystic duct (cholecystectomy)
    • Common bile duct (choledoectomy)
    • Head of the pancreas
    • Duodenum
    • Proximal jejunum
    • Regional lymph nodes

SURGERY

- Distal pancreatectomy
  - Removal of the body and tail of the pancreas and spleen
- Total pancreatectomy
  - Similar to a Whipple, but the entire pancreas is removed
  - Patient will be required to take supplemental enzymes and insulin

CHEMOTHERAPY/RADIATION

- Adjuvant Therapy
  - Chemotherapy
  - Chemoradiation
  - IMRT
- Neoadjuvant Therapy
  - Performed on patients that are borderline surgical candidates
  - Chemoradiation
CHEMOTHERAPY/RADIATION

• Primary Treatment
  • Intent is palliative and improved survival
• Chemotherapy
  • 5-FU & Gemcitabine
  • Clinical trials
• Chemoradiation
• Radiation
  • IMRT

RADIATION THERAPY

• Generally external beam, brachytherapy rare
• IMRT
  • Minimizes the dose to proximal healthy tissue
  • Fewer side effects & higher dose to tumor
• SBRT
  • Used with smaller tumors ("cyberknife")
  • Not better than standard; ulcers in duodenum
  • Still under investigation
• Proton beam
  • Clinical Trials
CHEMOTHERAPY

• Abrazane (albumin-bound paclitaxel)
• Gemzar (gemcitabine)—1996
  • Combined with radiation
  • Combined with Tarceva for metastatic
• 5-FU (flourouracial)—older; more often combo with radiation
• ONIVYDE (irinotecan liposome injection)—2013
  • 1st line treatment for metastatic; 3 drug combo

ABLATION OR EMBOLIZATION

• Primarily endocrine
  • Metastatic
  • Occasionally for exocrine if extension is only into a few areas
• Ablation
  • Destroy tumors with extreme heat or cold
  • No hospital stay
• Embolization
  • Inject substances into artery to block blood flow to tumor
  • Used for tumors too large for ablation
METASTATIC

• ONIVYDE (irinotecan liposome injection)
• Chemo—Gemcitabine
  • Alone if poor health
  • Otherwise combined
    • Albumin-bound paclitaxel, erlotinib, or cepectabine
• FOLFIRINOX—standard of care
  • 4 drug combo (5-FU, leucovorin, irinotecan, & oxaliplatin)
  • Must be in good health; side effects an issue

RECURRENT OR PROGRESSION

• Depends upon prior treatments
• Where & how much spread
• Emphasis on patient wishes
• Chemo (same or different)
  • Can be for treatment or palliative
• Radiation
  • Palliative
• Clinical Trials
PANCREATIC NET

- Surgery if resectable
- If not, lab and imaging used to monitor
  - Slow growing
  - Diarrhea or hormone problems
    - Treatment of symptoms also appear to slow growth of tumor
  - Chemo or targeted drugs (sunitinib or everolimus) usually delayed until symptoms are uncontrolled or scans show tumor growth
    - But first treatment if poorly differentiated tumor
    - Somatostatin receptor-positive PNET: radiopharmaceutical Lutathera (lutetium Lu 177 dotatate)
  - Ablation if spread to liver

AMPULLA OF VATER

- Symptomatic at earlier stage
  - Jaundice
- Surgery generally an option
  - Whipple followed by adjuvant chemoradiotherapy
- Advanced cases are treated like advance pancreatic cancer
CLINICAL TRIALS

- Recommended at diagnosis & during every treatment decision
  - 71% die within 1 year; outcomes “better” in clinical trial
  - 4.5% of patients enroll
- 181 NCI supported
  - 13 Phase 3
  - 15 Phase 4
- Pancreatic Cancer Action Network
  - Clinical Trial Finder

QUIZ 2
CASE SCENARIOS
Fabulous Prizes Winners

CE CERTIFICATE QUIZ/SURVEY

• Phrase

• Link

https://www.surveygizmo.com/s3/4288842/Pancreas-2018
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RECINDA SHERMAN  rsherman@naaccr.org