2021 Cancers - Upper GI Tract: Diagnosis, Workup, Staging, Treatment

2020-2021 FCDS ANNUAL WEBCAST SERIES
FEBRUARY 18, 2021
STEVEN PEACE, CTR

CDC & Florida DOH Attribution

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FCDS would also like to acknowledge the Florida Department of Health for its support of the Florida Cancer Data System, including the development, printing and distribution of materials for the 2020 FCDS Annual Conference and the 2020-2021 FCDS Webcast Series under state contract CODJU. The findings and conclusions in this series are those of the author(s) and do not necessarily represent the official position of the Florida Department of Health.
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Presentation Outline

- Introduction to the Upper GI Tract
- Introduction to the Biliary System and Biliary Tree
- Introduction to the Physiology of the Upper GI Tract and Biliary System
- Incidence and Mortality – Increasing Rates Gallbladder and Liver Cancers
- Latest Advances and Use of Endoscopic Ultrasound (EUS)
- Each Section Will Cover: Anatomy/Physiology/Risk Factors/Symptoms/Classification/ Diagnosis/ Staging/Treatment for;
  - Esophagus (including GE Junction)
  - Stomach (including GE Junction)
  - Biliary System (Biliary Tree)
    - Pancreas (Pancreatic Duct)
    - Gallbladder (Intrahepatic Bile Ducts & Common Bile Duct)
    - Liver (Hepatic Ducts)
  - Upper Duodenum
- Tumor Markers and Genetic Testing
- References
- Questions
Introduction to the Upper GI Tract

Cancers from these sites account for approximately 10% of all incident cancers – but, make up nearly 20% of all cancer deaths.

Introduction to the Upper GI Tract

What is upper gastrointestinal (upper GI) cancer?

- Seven main types of upper gastrointestinal (Upper GI) cancer: esophageal, stomach, pancreatic, duodenal, gall bladder and bile duct, liver and small bowel cancers.

- **Esophageal cancer** - This can develop anywhere along the length of the esophagus (gullet/‘food pipe’). Two common types are adenocarcinoma of the esophagus, and squamous cell carcinoma. These are named after the type of cells they originate from.

- **Stomach cancer** - Most stomach cancers develop in cells lining the stomach. This type of cancer is called an adenocarcinoma of the stomach. This usually develops slowly. Other stomach cancers include gastrointestinal stromal tumors (GISTs) or neuroendocrine tumors (NETs). These are relatively rare and can occur anywhere in the gastrointestinal tract (digestive system).

- **Pancreatic cancer** - The pancreas produces insulin and digestive enzymes. It sits below the stomach and has a duct which allows the enzymes which it produces to enter the duodenum (the first part of the small bowel). The pancreas is divided into head, neck, body and tail which all have different roles. Cancer can occur in any area.
Introduction to the Upper GI Tract

What is upper gastrointestinal (upper GI) cancer?

- Seven main types of upper gastrointestinal (Upper GI) cancer: esophageal, stomach, pancreatic, duodenal, gall bladder and bile duct, liver and small bowel cancers.

- **Duodenal cancer** - The duodenum is the first part of the small intestine (bowel) below the stomach. Foods which have been mixed with stomach acid in the stomach are then released into the duodenum where they are mixed with bile (made in the liver and stored in the gall bladder) and with digestive juices from the pancreas. Duodenal cancer is relatively rare compared to stomach (gastric) cancer and colorectal cancer.

- **Biliary tract or gallbladder cancer** - This develops either in the gall bladder itself, or in the system of tubes which bring the bile ('gall') which the gallbladder stores, to the duodenum where it is used in the digestive process.

- **Liver cancer** – Primary liver cancer develops from liver cells that have become malignant. It is also possible to get secondary liver cancer, which is where cancers in other organs then spread (metastasis) to the liver. These are called by the name of the original ('primary') cancer - e.g. 'pancreatic cancer metastases in the liver'.

Introduction to Biliary System/Tree
There are three important functions of the biliary system, these include:

- Draining the waste products from the liver (into the duodenum)
- Secreting bile in a controlled release manner
- Transporting bile and pancreatic juices (to be used to help breakdown food in the small intestine)
Observing Rising Trends in Mortality

**Observing Rising Trends in Mortality**

**Trends in Cancer Death Rates** Among Males, US, 1930-2018

**Trends in Cancer Death Rates** Among Females, US, 1930-2018

Endoscopic Ultrasound (EUS)

- Endoscopy refers to the procedure of inserting a long flexible tube via the mouth or the rectum to visualize the digestive tract. For further information, please visit the Colonoscopy and Flexible Sigmoidoscopy articles. Whereas ultrasound uses high-frequency sound waves to produce images of the organs and structures inside the body such as ovaries, uterus, liver, gallbladder, pancreas, or aorta.

- **Endoscopic Ultrasound (EUS)** combines endoscopy and ultrasound in order to obtain images and information about the digestive tract and the surrounding tissue and organs.

- In EUS a small ultrasound transducer is installed on the tip of the endoscope. By inserting the endoscope into the upper or the lower digestive tract one can obtain high quality ultrasound images of the organs inside the body. Placing the transducer on the tip of an endoscope allows the transducer to get close to the organs inside the body. Because of the proximity of the EUS transducer to the organ(s) of interest, the images obtained are frequently more accurate and more detailed than the ones obtained by traditional ultrasound. The EUS also can obtain information about the layers of the intestinal wall as well as adjacent areas such as lymph nodes and the blood vessels.

- EUS plays an important role in the diagnosis of pancreatic cancer, including FNA with cytological or histological confirmation. Staging of pancreatic cancer is crucial and CT and EUS are the cornerstones of staging, currently providing the more accurate results. Furthermore, EUS also has a therapeutic role, providing biliary drainage when it is not feasible with ERCP and pain relief. EUS can also have future applications on pancreatic cancer management.
### Endoscopic Ultrasound (EUS)

Prospective retrospective studies on diagnostic performance of EUS versus CT for detection of pancreatic malignancy

<table>
<thead>
<tr>
<th>Study</th>
<th>Year</th>
<th>EUS vs CT</th>
<th>CT vs EUS</th>
<th>Na</th>
<th>Na</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kamata et al.</td>
<td>2014</td>
<td>35</td>
<td>100 vs 38*</td>
<td>100 vs 100</td>
<td>NA</td>
</tr>
<tr>
<td>Kikuchi et al.</td>
<td>2012</td>
<td>277</td>
<td>91 vs 71*</td>
<td>94 vs 92</td>
<td>NA</td>
</tr>
<tr>
<td>Sakamoto et al.</td>
<td>2008</td>
<td>136</td>
<td>94 vs 58*</td>
<td>NA</td>
<td>NA</td>
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<tr>
<td>Kano et al.</td>
<td>2008</td>
<td>42</td>
<td>100 vs 88*</td>
<td>89 vs 83</td>
<td>NA</td>
</tr>
<tr>
<td>Kikuchi et al.</td>
<td>2004</td>
<td>65</td>
<td>91 vs 68*</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Asamura et al.</td>
<td>2004</td>
<td>81</td>
<td>100 vs 75*</td>
<td>NA</td>
<td>94 vs 74*</td>
</tr>
<tr>
<td>Defilippi et al.</td>
<td>2004</td>
<td>81</td>
<td>100 vs 75*</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Ricciardone et al.</td>
<td>2003</td>
<td>48</td>
<td>100 vs 48*</td>
<td>75 vs 50*</td>
<td>98 vs 67*</td>
</tr>
<tr>
<td>Metz et al.</td>
<td>2000</td>
<td>35</td>
<td>93 vs 53*</td>
<td>NA</td>
<td>85 vs 49*</td>
</tr>
<tr>
<td>Gross et al.</td>
<td>1999</td>
<td>131</td>
<td>100 vs 74</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Harrison et al.</td>
<td>1999</td>
<td>19</td>
<td>100 vs 50*</td>
<td>NA</td>
<td>98 vs 63*</td>
</tr>
<tr>
<td>Maltrey et al.</td>
<td>1999</td>
<td>48</td>
<td>97 vs 76</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Leggans et al.</td>
<td>1998</td>
<td>50</td>
<td>100 vs 92</td>
<td>NA</td>
<td>93 vs 93</td>
</tr>
<tr>
<td>Sugiyama et al.</td>
<td>1997</td>
<td>48</td>
<td>96 vs 89*</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Howard et al.</td>
<td>1997</td>
<td>21</td>
<td>75 vs 83*</td>
<td>77 vs 100*</td>
<td>76 vs 86*</td>
</tr>
<tr>
<td>Maloney et al.</td>
<td>1996</td>
<td>12</td>
<td>100 vs 83</td>
<td>NA</td>
<td>100 vs 96</td>
</tr>
<tr>
<td>Nakamura et al.</td>
<td>1995</td>
<td>232</td>
<td>94 vs 65*</td>
<td>97 vs 94</td>
<td>96 vs 88*</td>
</tr>
<tr>
<td>Marti et al.</td>
<td>1995</td>
<td>37</td>
<td>92 vs 63</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Miller et al.</td>
<td>1994</td>
<td>49</td>
<td>94 vs 69*</td>
<td>100 vs 64</td>
<td>98 vs 67</td>
</tr>
<tr>
<td>Palazzo et al.</td>
<td>1993</td>
<td>64</td>
<td>96 vs 69*</td>
<td>73 vs 53</td>
<td>91 vs 66*</td>
</tr>
<tr>
<td>Yoshida et al.</td>
<td>1993</td>
<td>29</td>
<td>100 vs 72*</td>
<td>NA</td>
<td>Duodenal invasion: 85 vs 32</td>
</tr>
<tr>
<td>Risch et al.</td>
<td>1991</td>
<td>102</td>
<td>99 vs 77</td>
<td>100 vs 53</td>
<td>NA</td>
</tr>
</tbody>
</table>

*Statistically significant data. Statistics are not available.
Endoscopic Ultrasound (EUS)

RCT comparing EUS-FNA and EUS-FNB for diagnosis of pancreatic cancer

<table>
<thead>
<tr>
<th>Study</th>
<th>Year of study</th>
<th>Total no. of patients</th>
<th>Accuracy-diagnostic yield, FNA versus FNB (%)</th>
<th>Sensitivity, FNA versus FNB (%)</th>
<th>Specificity, FNA versus FNB (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Cheng et al.</td>
<td>2018</td>
<td>408</td>
<td>80 vs 91.4*</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Van Riet et al.</td>
<td>2019</td>
<td>608</td>
<td>87 vs 78*</td>
<td>90 vs 82*</td>
<td>96 vs 91</td>
</tr>
<tr>
<td>Wang et al.</td>
<td>2016</td>
<td>408</td>
<td>80 vs 90</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Vachier-Lab袴 et al.</td>
<td>2014</td>
<td>80</td>
<td>92.5 vs 90</td>
<td>NA</td>
<td>NA</td>
</tr>
<tr>
<td>Lee et al.</td>
<td>2014</td>
<td>118</td>
<td>94.8 vs 98.3</td>
<td>94.6 vs 98.2</td>
<td>100 vs 100</td>
</tr>
<tr>
<td>Strand et al.</td>
<td>2014</td>
<td>32</td>
<td>93.8 vs 28.1*</td>
<td>NA</td>
<td>NA</td>
</tr>
</tbody>
</table>

*Statistically significant data.

EUS, endoscopic ultrasound; FNA, fine-needle aspiration; FNB, fine-needle biopsy; NA, not applicable; RCT, randomized control trial.

Diagnostic Confirmation Review

<table>
<thead>
<tr>
<th>Code</th>
<th>Description</th>
<th>Definition</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>Positive histology</td>
<td>Histologic confirmation (tissue microscopically examined).</td>
</tr>
<tr>
<td>2</td>
<td>Positive cytology</td>
<td>Cytologic confirmation (no tissue microscopically examined; fluid cells microscopically examined).</td>
</tr>
<tr>
<td>4</td>
<td>Positive microscopic confirmation, method not specified</td>
<td>Microscopic confirmation is all that is known; the estimation if the cells were from histology or cytology.</td>
</tr>
<tr>
<td>5</td>
<td>Positive laboratory test/marker study</td>
<td>A clinical diagnosis of cancer is based on laboratory test/marker studies which are clinically diagnostic for cancer. Examples include serum beta-HCG for germ cell tumors and abnormal electrophoretic alpha-fetoprotein for multiple myeloma. Elevated PSA is not diagnostic of cancer; if the physician uses the PSA as a basis for diagnosing prostate cancer with no other workup, record as code 5.</td>
</tr>
<tr>
<td>6</td>
<td>Direct visualization without microscopic confirmation</td>
<td>The tumor was visualized during a surgical or endoscopic procedure only with no tissue resected for microscopic examination.</td>
</tr>
<tr>
<td>7</td>
<td>Radiography and other imaging techniques without microscopic confirmation</td>
<td>The malignancy was reported by the physician from an imaging technique report only.</td>
</tr>
<tr>
<td>8</td>
<td>Clinical diagnosis only, other than 5, 6 or 7</td>
<td>The malignancy was reported by the physician in the medical record.</td>
</tr>
<tr>
<td>9</td>
<td>Unknown whether or not microscopically confirmed</td>
<td>A statement of malignancy was reported in the medical record, but there is no statement of how the cancer was diagnosed (usually nonanalytic).</td>
</tr>
</tbody>
</table>
## Behavior of Tumor on EUS

<table>
<thead>
<tr>
<th>Reportable</th>
<th>ICD-O-3</th>
<th>Description</th>
</tr>
</thead>
<tbody>
<tr>
<td>Yes</td>
<td>8350/2</td>
<td>All Histologies with Behavior Code of /2 (in-situ)</td>
</tr>
<tr>
<td>Yes</td>
<td>8350/3</td>
<td>Invasive Duct Carcinoma of the pancreas</td>
</tr>
<tr>
<td>Yes</td>
<td>8150/3</td>
<td>Cystic Pancreatic Endocrine Neoplasm (CPEN)</td>
</tr>
<tr>
<td>Yes</td>
<td>8500/3</td>
<td>Intraductal Oncocytic Papillary Neoplasm (IOPN) of the pancreas</td>
</tr>
<tr>
<td>Yes</td>
<td>8453/2</td>
<td>Intraductal Papillary Mucoepidermoid Carcinoma of the pancreas</td>
</tr>
<tr>
<td>Yes</td>
<td>8503/2</td>
<td>Intraductal Tubule-Papillary Neoplasm (ITPN) of the pancreas</td>
</tr>
<tr>
<td>Yes</td>
<td>8503/3</td>
<td>Intraductal Tubule-Papillary Neoplasm (ITPN) with invasive carcinoma</td>
</tr>
<tr>
<td>Yes</td>
<td>8470/2</td>
<td>Cystadenocarcinoma of the pancreas</td>
</tr>
<tr>
<td>Yes</td>
<td>8470/3</td>
<td>Mucinous Cystadenocarcinoma of the pancreas</td>
</tr>
<tr>
<td>Yes</td>
<td>8470/2</td>
<td>Mucinous Cystadenocarcinoma, non-invasive (MCN)</td>
</tr>
<tr>
<td>Yes</td>
<td>8470/3</td>
<td>Mucinous Cystadenocarcinoma of the pancreas</td>
</tr>
<tr>
<td>Yes</td>
<td>8246/3</td>
<td>Neuroendocrine Tumor, Grade 1 (NET GR1) of the pancreas</td>
</tr>
<tr>
<td>Yes</td>
<td>8249/3</td>
<td>Neuroendocrine Tumor, Grade 2 (NET GR2) of the pancreas</td>
</tr>
<tr>
<td>Yes</td>
<td>8471/3</td>
<td>Papillary Mucinous Pancreatic Neoplasm (PAN) of the pancreas</td>
</tr>
<tr>
<td>Yes</td>
<td>8552/3*</td>
<td>Mixed acinar-ductal carcinoma</td>
</tr>
<tr>
<td>Yes</td>
<td>8163/2*</td>
<td>Papillary neoplasm, pancreatoatypical-type, with high grade intraepithelial neoplasia</td>
</tr>
<tr>
<td>Yes</td>
<td>8163/3*</td>
<td>Pancreatoatypical-type carcinoma</td>
</tr>
<tr>
<td>No</td>
<td>n/a</td>
<td>Histologies with Behavior Code of /0 (benign)</td>
</tr>
<tr>
<td>No</td>
<td>n/a</td>
<td>Histologies with Behavior Code of /1 (borderline)</td>
</tr>
</tbody>
</table>

* New histology codes not yet implemented in the U.S. are still reportable – use histology 8500 or 8140

Esophagus (including GE Junction) Anatomy/Physiology

The Esophagus

• Moves food from the pharynx down to the stomach.
• Movement of food, now called a bolus, is not dependent on gravity.
• Dependent on peristalsis, the rhythmic contraction of smooth muscle that moves the bolus down to the stomach.
• At the distal esophagus, food must pass through the lower esophageal sphincter before entering the stomach.
• This structure generally forbids stomach contents from moving backward into the esophagus.
• If it does, this causes acid reflux.
• Additionally, the epiglottis prevents food from moving into the trachea (respiratory tract).
• The bolus pushes the glottis down, covering the opening to the trachea.

Esophagus (including GE Junction) Anatomy/Physiology

[Diagrams of esophagus anatomy and physiology]
Esophagus (including GE Junction)

**Risk Factors/Symptoms**

**Risk Factors Include:**
- Age > 55
- Male
- Tobacco and Alcohol Use – risk for both squamous and adenocarcinoma of the esophagus
- Gastroesophageal Reflux Disease – GERD
- Barrett’s Esophagus
- Obesity
- Diet
- Physical Activity
- Injury to Esophagus – for example exposure to lye in cleaning products or drinking toxic chemicals
- HPV infection
- Acquired Gene Mutations – from one of the other conditions above
- Inherited Gene Mutations – Tylosis (Howel-Evans Syndrome), Bloom Syndrome, Fanconi Anemia, Familial Barrett’s Esophagus

**Symptoms Include:**
- Trouble swallowing
- Chest pain
- Weight loss
- Hoarseness
- Chronic cough
- Vomiting
- Bone pain (if cancer has spread to the bone)
- Bleeding into the esophagus.

Esophagus (including GE Junction)

**WHO 5th edition Classification of Neoplasms of Pancreas**

**Epithelial Tumors**

- Benign epithelial tumors and precursors
  - Esophageal squamous papilloma
  - Barrett dysplasia
  - Esophageal squamous dysplasia

- Malignant epithelial tumors
  - Adenocarcinoma of the esophagus and esophagogastric junction NOS
  - Esophageal adenoid cystic carcinoma
  - Esophageal adenocarcinoma and mucinous carcinoma
  - Esophageal squamous cell carcinoma NOS
  - Esophageal undifferentiated carcinoma
  - Esophageal neuroendocrine neoplasms
Esophagus (including GE Junction) Diagnosis/Staging

- Screening of High Risk Groups
- Screening in High Risk Geographic Areas
- Diagnostic Imaging
- Barium Swallow
- Upper Endoscopy
- Endoscopic Ultrasound
- Bronchoscopy
- Thoracoscopy and Laparoscopy
- Labs: CBC, Liver Enzymes, HER2, PD-L1, MMR, MSI

Esophagus (including GE Junction) Treatment

- Treating for Barrett's Esophagus to find early disease
- Endoscopic Treatments
  - Endoscopic mucosal resection
  - Photodynamic therapy
  - Radiofrequency ablation
- Surgery – esophagectomy (depends on location of primary), nodes
- Palliative Surgery – to relieve symptoms
- Radiation – External Beam (IMRT) or Brachytherapy (high or low dose)
- Chemotherapy – neoadjuvant (pre-surgical), adjuvant (post-surgical)
- Targeted Therapies
- Immunotherapy
- Combination therapy
Stomach (including GE Junction) Anatomy/Physiology

Regions of the stomach

- Cardia
- Body
- Fundus
- Pylorus
- Antrum
- Duodenum
- Pyloric sphincter
- Rugae
- Greater curvature
- Lesser curvature
- Circular muscle layer
- Longitudinal muscle layer
- Mucosa
- Muscularis mucosa
- Submucosa
- Oblique muscle layer
- Muscularis
- Connective tissue layer
- Serosa

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Stomach (including GE Junction) Anatomy/Physiology

Normal esophagus

Barrett's esophagus

Risk factors:
- Male
- Caucasian
- Obesity
- Increased age
- Smoking

Normal esophagus
- Barrett's esophagus
- Pre-cancerous changes
- Low grade dysplasia
- High grade dysplasia
- Cancer
Stomach (including GE Junction)
Risk Factors/Symptoms

- Gender – more common in men than women
- Age – sharp increase in rates over age 50 but most diagnosed in late 60’s-80’s
- Ethnicity – more common in Hispanic Americans, African Americans, Native Americans, and Asian/Pacific Islanders than it is in non-Hispanic whites.
- Geography - more common in Japan, China, Southern and Eastern Europe, and South and Central America. This disease is less common in Northern and Western Africa, South Central Asia, and North America
- Helicobacter pylori infection - Infection with Helicobacter pylori (H pylori) bacteria seems to be a major cause of stomach cancer, especially cancers in the lower (distal) part of the stomach. Long-term infection of the stomach with this germ may lead to inflammation (called chronic atrophic gastritis) and pre-cancerous changes of the inner lining of the stomach. People with stomach cancer have a higher rate of H pylori infection than people without this cancer. H pylori infection is also linked to some types of lymphoma of the stomach.
- Stomach Lymphoma – Persons with MALT lymphoma have an increased risk of getting adenocarcinoma of the stomach. This is probably because MALT lymphoma of the stomach is caused by infection with H pylori bacteria.
- EBV Infection - Epstein-Barr virus causes infectious mononucleosis (also called mono). EBV has been linked to some forms of lymphoma. It is also found in the cancer cells of about 5% to 10% of people with stomach cancer. These people tend to have a slower growing, less aggressive cancer with a lower tendency to spread.
- Diet/Obesity/Overweight/Inactivity – large amounts of smoked foods, salted fish and meat, and pickled vegetables
- Type A Blood
- Menetrier Disease – hypertrophic gastropathy
- Pernicious Anemia – vitamin B12 deficiency
- Occupation – coal, metal and rubber industries at risk
- Familial Syndromes – Li-Fraumeni, Peutz-Jeghers, Lynch Syndrome (HNPCC), family history of stomach cancer
- FAP/BRCA1/BRCA2
- Tobacco Use

Stomach (including GE Junction)
WHO 5th edition Classification of Neoplasms of Pancreas

Tumors of the stomach

- Epithelial tumors
  - Benign epithelial tumors and precursors
    - Fundic gland polyps
    - Gastric hyperplastic polyps
    - Gastric dysplasia
    - Intestinal-type gastric adenoma
    - Foveolar-type adenoma
    - Gastric pyloric gland adenoma
    - Oxyntic gland adenoma
  - Malignant epithelial tumors
    - Gastric adenocarcinoma
    - Gastric squamous cell carcinoma
    - Gastric adenosquamous carcinoma
    - Gastric undifferentiated carcinoma
    - Gastroblastoma
    - Gastric neuroendocrine neoplasms
- Mesenchymal tumors
  - Gastrointestinal Stromal Tumor (GIST)
  - MALT Lymphoma and Leiomyosarcoma
### Stomach (including GE Junction) Diagnosis/Staging

- Medical History and Physical Exam – pain, bloating, acid stomach
- Test for Helicobacter Pylori Infection
- Upper Endoscopy – for Screening and for Diagnosis
- Endoscopic Ultrasound
- Diagnostic Imaging
- Upper GI Series – barium swallow uses x-rays – single or double contrast
- Biopsy (includes testing of biopsy material by IHC and FISH for HER2, PD-L1, etc)
- Sentinel Node Mapping
- Laparoscopy

<table>
<thead>
<tr>
<th>SEER stage</th>
<th>5-year relative survival rate</th>
</tr>
</thead>
<tbody>
<tr>
<td>Localized</td>
<td>65%</td>
</tr>
<tr>
<td>Regional</td>
<td>31%</td>
</tr>
<tr>
<td>Distant</td>
<td>5%</td>
</tr>
</tbody>
</table>

### Stomach (including GE Junction) Treatment

- Antibiotics to prevent cancer in patients with H pylori
- NSAIDS – not proven but suggestion that these may help prevent cancer
- Screening Tests to identify early disease and treat it before it becomes cancer
- Endoscopic Resection
- Open Surgery – depends on primary tumor location and imaging results
- Open Surgery – total gastrectomy, subtotal gastrectomy, esophagogastrectomy
- Palliative Surgery for Unresectable Cancer – Gastric Bypass, Tumor Ablation, Stent
- Chemotherapy – neoadjuvant, adjuvant
- Targeted Therapies – HER2 (Trastuzumab/Herceptin, EGFR (Panitumumab)
- Immunotherapy – Pembrolizumab/Keytruda – targets PD-L1 – checkpoint inhibitor
- Radiation Therapy – External Beam
Introduction
Pancreato-Hepato-Biliary System

Pancreas (Pancreatic Duct) Anatomy/Physiology
Pancreas (Pancreatic Duct)

Risk Factors/Symptoms

**Risk Factors**

- Tobacco Use
- Obesity/Overweight/Inactivity
- Type 2 Diabetes
- Chronic Pancreatitis – long term inflammation of pancreas seen in folks with heavy smoking and/or heavy drinking history or current use
- Workplace Chemical Exposures – dry cleaning and metal working
- Age >65
- Male
- African American – may be due to other risk factors
- Family History & Inherited Genetic Syndromes
- Acquired Gene Mutations due to exposures above

**Symptoms**

- Jaundice – yellowing of eyes and skin

**Acute pancreatitis symptoms include:**

- Upper abdominal pain
- Abdominal pain that radiates to your back
- Abdominal pain that feels worse after eating
- Fever
- Rapid pulse
- Nausea
- Vomiting
- Tenderness when touching the abdomen

**Chronic pancreatitis symptoms include:**

- Upper abdominal pain
- Losing weight without trying
- Oily, smelly stools (steatorrhea)

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Pancreas (Pancreatic Duct)

WHO 5th edition Classification of Neoplasms of Pancreas

**Epithelial Tumors**

- Benign epithelial tumors and precursors
  - Acinar cystic transformation of the pancreas
  - Serous neoplasms of the pancreas
  - Pancreatic intraepithelial neoplasia
  - Pancreatic intraductal papillary mucinous neoplasm
  - Pancreatic intraductal oncocytic papillary neoplasm
  - Pancreatic intraductal tubulopapillary neoplasm
  - Pancreatic mucinous cystic neoplasm

- Malignant epithelial tumors
  - Pancreatic ductal adenocarcinoma
  - Pancreatic acinar cell carcinoma
  - Pancreatoblastoma
  - Solid pseudopapillary neoplasm of the pancreas

**Precursor Lesions**

- Serous cystic neoplasms (SCNs) (also known as serous cystadenomas) are tumors that have sacs (cysts) filled with fluid. SCNs are almost always benign, and most don’t need to be treated.
- Mucinous cystic neoplasms (MCNs) (also known as mucinous cystadenomas) are slow-growing tumors that have cysts filled with a jelly-like substance called mucin. These tumors can progress to cancer over time if not treated, so these tumors are typically removed with surgery.
- Intraductal papillary mucinous neoplasms (IPMNs) are benign tumors that grow in the pancreatic ducts. Like MCNs, these tumors make mucin, and over time they sometimes become cancer if not treated.
- Solid pseudopapillary neoplasms (SPNs) are rare, slow-growing tumors that develop in young women. Even though these tumors tend to grow slowly, they can sometimes spread to other parts of the body, so they are best treated with surgery.
Pancreatic Neuroendocrine Neoplasms

- Pancreatic neuroendocrine neoplasms: Introduction
- Non-functioning pancreatic neuroendocrine tumors
- Functioning pancreatic neuroendocrine tumors
  - Insulinoma
  - Gastrinoma
  - VIPoma
  - Glucagonoma
  - Somatostatinoma
  - ACTH-producing neuroendocrine tumor
  - Serotonin-producing neuroendocrine tumor
- Pancreatic neuroendocrine carcinoma
- Pancreatic MiNEs

Pancreas (Pancreatic Duct)

Diagnosis/Staging

- Medical History and Physical Exam
- Diagnostic Imaging – typical (CT, MRI, PET, Ultrasound)
- Cholangiopancreatography – a specialized imaging test
- Magnetic resonance cholangiopancreatography (MRCP)
- Percutaneous transhepatic cholangiography (PTC)
- Liver Function Tests
- Tumor Markers – CA19-9 and CEA – neither are every diagnostic – alone
- Biopsy – percutaneous, endoscopic, surgical
- Genetic Testing – BRCA1, BRCA2, NTRK – targeted drugs available

<table>
<thead>
<tr>
<th>SEER Stage</th>
<th>5-year Relative Survival Rate</th>
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<tr>
<td>Localized</td>
<td>37%</td>
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<tr>
<td>Regional</td>
<td>12%</td>
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<tr>
<td>Distant</td>
<td>3%</td>
</tr>
<tr>
<td>All SEER stages combined</td>
<td>9%</td>
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</table>
Pancreas (Pancreatic Duct) Treatment

- Staging Laparoscopy
- Tumor Ablation or Embolization of Primary Tumor or Metastasis
- Surgery – Distal Pancreatectomy – removes tail of pancreas and some of body
- Surgery – Total Pancreatectomy – removes entire pancreas and gallbladder, part of stomach and small intestine and the spleen
- Surgery – Whipple Procedure – Pancreaticoduodenectomy – most common
- Surgery – palliative to reduce symptoms – less extensive or bypass surgery
- Radiation Therapy – External Beam Radiation
- Chemotherapy – neoadjuvant, adjuvant, palliative
- Targeted Therapy – Erlotinib/Tarceva (EGFR Inhibitor), Olaparib/Lynparza (PARP Inhibitor), Larotrectinib/Vitrakvi and Entrectinib/Rozyltrek (NTRK proteins/gene mutations)
- Immunotherapy – Immune Checkpoint Inhibitors (Keytruda/Pembrolizumab – PD-1 Inhibitor)
- Pain Control Only – opioids including morphine

Liver (Hepatic Ducts) Anatomy/Physiology
Liver (Hepatic Ducts)
Risk Factors/Symptoms

- Male
- Asian Americans and Pacific Islanders
- Hispanics/Latinos, American Indians/Alaska Natives
- African Americans and Whites
- Chronic Viral Hepatitis (HBV or HCV)
- Cirrhosis
- Non-Alcoholic Fatty Liver Disease
- Primary Biliary Cirrhosis
- Heavy Alcohol Use & Tobacco Use
- Obesity
- Type 2 Diabetes
- Exposure to Allatoxins – fungus that contaminates peanuts, wheat, soybeans, ground nuts, corn and rice from poor storage practices
- Exposure to Vinyl Chloride / Thorium Dioxide (Thorotrast)
- Long-Term Anabolic Steroid Use

- Weight loss (without trying)
- Loss of appetite
- Feeling very full after a small meal
- Nausea or vomiting
- An enlarged liver, felt as fullness under the ribs on the right side
- An enlarged spleen, felt as fullness under the ribs on the left side
- Pain in the abdomen (belly) or near the right shoulder blade
- Swelling or fluid build-up in the abdomen (belly)
- Itching
- Yellowing of the skin and eyes (jaundice)

Liver (Hepatic Ducts)
WHO 5th edition Classification of Neoplasms of Pancreas

Epithelial Tumors

- Benign hepatocellular tumors
  - Focal nodular hyperplasia of the liver
  - Hepatocellular adenoma
- Malignant hepatocellular tumors and precursors
  - Hepatocellular carcinoma
  - Hepatoblastoma
- Benign biliary tumor’s and precursors
  - Bile duct adenoma
  - Biliary adenofibroma
  - Biliary intraepithelial neoplasia (See chapter 9)
  - Intraductal papillary neoplasm of the bile ducts (See chapter 9)
  - Mucinous cystic neoplasm of the liver and biliary system
- Malignant biliary tumors
  - Intrahepatic cholangiocarcinoma
  - Combined hepatocellular-cholangiocarcinoma and undifferentiated primary liver carcinoma
  - Hepatic neuroendocrine neoplasms
"Cholangiocarcinoma"
A loosely used term...

Liver (Hepatic Ducts)
Diagnosis/Staging

- Prevention
- Medical History and Physical Exam
- Screening for Hepatitis B and Hepatitis C
- Lab Tests with AFP and other proteins in the blood
- Liver Function Tests & Kidney Function Tests
- Ultrasound
- Imaging – CT/MRI/PET/Bone Scan/Angiography
- Fibrosis Score – indicates whether or not transplant is an option to treat
- Biopsy – FNA, Laparoscopic, Surgical Biopsy

Cancer Staging Systems
- UICC/AJCC TNM Staging System
- The Barcelona Clinic Liver Cancer (BCLC) system
- The Cancer of the Liver Italian Program (CLIP) system
- The Okuda system
- Child-Pugh Score – cirrhosis staging
Liver (Hepatic Ducts) Treatment

- Surgery - resectable, transplantable, unresectable, inoperable
- Surgery – partial hepatectomy
- Surgery - liver transplant
- Chemoembolization/Radioembolization – infuse chemo/xrt beads and seal them off with embolization
- Chemotherapy – Gemcitabine, Oxaliplatin, Cisplatin, Doxorubicin, 5-FU, Capecitabine, Mitoxantrone
- Ablation Therapy – RFA, MWA, Cryoablation, Ethanol Ablation
- Trans-arterial embolization (TAE)
- Trans-arterial chemoembolization (TACE)
- Drug-eluting Bead Chemoembolization (DEB-TACE)
- Radioembolization
- Targeted Therapy – Nexavar/sorafenib – Kinase Inhibitor - inhibits blood vessel growth
- Targeted Therapy – Cyramza/ramucirumab – Monoclonal Antibody – same as above
- Targeted Therapy – Monoclonal Antibodies – Beevacizumab/Avastin
- Virus Therapy – JX-594 – same virus used to make smallpox vaccine
- Immunotherapy – PD-1 and PD-L1 Inhibitors and CTLA-4 Inhibitor - Yervoy

Gallbladder (Intrahepatic Bile Ducts & Common Bile Duct) Anatomy/ Physiology
**Gallbladder (Intrahepatic Bile Ducts & Common Bile Duct)**

**Risk Factors/Symptoms**
- Medical History of Chronic Infection and Inflammation
- Primary Sclerosing Cholangitis (PSC)
- Bile Duct Stones
- Choledochal Cyst Disease
- Liver Fluke Infections
- Cirrhosis
- Abnormalities Involving Junction of Bile Duct and Pancreatic Duct Anatomy
- Infection with Hepatitis B and/or Hepatitis B
- HIV Infection
- Chronic Pancreatitis and History of Gallstones
- Inflammatory Bowel Disease – ulcerative colitis, Crohn’s disease
- Hispanic Americans, Southeast Asia and China residents (liver flukes)
- Non-alcoholic Fatty Liver Disease
- Age > 60
- Obesity
- Diabetes
- Alcohol & Tobacco Abuse
- Exposure to asbestos, radon, PCBs, nitrosamines, chemicals used in rubber and textile industry

**Symptoms**
- Jaundice
- Itching
- Light-colored/Greasy Stools
- Dark Urine
- Abdominal Pain
- Loss of Appetite / Weight Loss
- Fever
- Nausea & Vomiting

**WHO 5th edition Classification of Neoplasms of Pancreas**

**Epithelial Tumors**
- Benign epithelial tumors and precursors
  - Pyloric gland adenoma of the gallbladder
  - Biliary intraepithelial neoplasia
  - Intracholecystic papillary neoplasm
    - formerly Intracystic / intraductal papillary neoplasm
    - intraductal papillary neoplasm of the bile ducts
- Malignant epithelial tumors
  - Carcinoma of the gallbladder
  - Carcinoma of the extrahepatic bile ducts
  - Neuroendocrine neoplasms of the gallbladder and bile ducts
Gallbladder (Intrahepatic Bile Ducts & Common Bile Duct) Diagnosis/Staging

- Screening High Risk Populations
- Medical History and Physical Exam
- Lab Tests of liver and gallbladder function
- Tumor Markers – CEA, CA19-9 (not diagnostic confirmation = 5)
- Imaging – Ultrasound, EUS, Laparoscopic, CT, MRI, Cholangiography, MRI Cholangiopancreatography (MRCP), Endoscopic Retrograde Cholangiopancreatography (ERCP), Percutaneous Transhepatic Cholangiography (PTC), Angiography
- Biopsy – various types and approaches
- Assess Resectable or Unresectable Disease

Gallbladder (Intrahepatic Bile Ducts & Common Bile Duct) Treatment

- Pre-Surgical Laparoscopy to plan for surgery
- Surgery – curative or palliative/resectable or unresectable
  - Simple Cholecystectomy
  - Laparoscopic Cholecystectomy
  - Open Cholecystectomy
  - Extended Cholecystectomy/Radical Cystectomy
- Liver Transplant or Tumor Ablation (RFA or Cryo), Photodynamic Therapy and Embolization
- Radiation Therapy – External Beam (IMRT), 3D Conformal, Stereotactic XRT, Brachytherapy
- Chemotherapy – adjuvant chemo, primary treatment chemo, palliative chemo, chemoradiation
- Chemotherapy – Hepatic Artery Infusion (HAI)
- Targeted Therapy – Pemigatinib (Pemazyre) – FGFR2 inhibitor for bile duct cancers only
- Immunotherapy – not available
- Palliative Therapy – code it if it is first course treatment – bypass surgery, stents, chemo, etc.
Upper Duodenum Anatomy/Physiology

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Upper Duodenum Risk Factors/Symptoms

- Male
- Age>60
- African American
- Smoking & Alcohol
- Diet – red meat, salted or smoked foods
- Celiac Disease
- Colon Cancer
- Crohn’s Disease
- Inherited Syndromes
  - Familial Adenomatous Polyposis (FAP)
  - Lynch Syndrome (hereditary nonpolyposis colorectal cancer or HNPCC)
  - Peutz-Jeghers Syndrome
  - MUTYH-Associated Polyposis
  - Cystic Fibrosis

- Pain in the belly (abdomen)
- Nausea and vomiting
- Weight loss (without trying)
- Weakness and feeling tired (fatigue)
- Dark-colored stools (bleeding in the intestine)
- Low red blood cell counts (anemia)
- Yellowing of the skin and eyes (jaundice)
Upper Duodenum
WHO 5th edition Classification of Neoplasms of Duodenum

Epithelial Tumors

- Benign epithelial tumors and precursors
  - Non-ampullary adenoma
  - Ampullary adenoma

- Malignant epithelial tumors
  - Non-ampullary adenocarcinoma
  - Ampullary adenocarcinoma
  - Small intestinal and ampullary neuroendocrine neoplasms

Range of hematolymphoid tumors including but not limited to:

- Extranodal MALT lymphoma of digestive tract
- Duodenal-type follicular lymphoma
- Enteropathy-associated T-cell lymphoma
- Monomorphic epitheliotropic intestinal T-cell lymphoma
- Intestinal T-cell lymphoma NOS
- Indolent T-cell lymphoproliferative disorder of the GI tract

Upper Duodenum
Diagnosis/Staging

- Medical History and Physical Exam
- Screening for individuals at high risk due to inherited genetic syndromes
- Imaging – CT, MRI, PET
- Upper GI Series
- Enteroclysis/CT Enteroclysis/MRI
- Enteroclysis – Detailed Upper GI Series
- Barium Enema
- CT-Guided Needle Biopsy
- Endoscopy – Capsule Endoscopy, Double-Balloon Enteroscopy
- Biopsy
- Labs for Mismatch Repair (MMR) and Microsatellite Instability (MSI)
Upper Duodenum Treatment

- Surgery – depends on resectable or unresectable cancer
- Surgery – segmental resection
- Surgery – Whipple Procedure (pancreaticoduodenectomy)
- Surgery – Palliative for pain control includes bypass surgery
- Chemotherapy – Capecitabine, 5-FU, Oxaliplatin, Irinotecan
- Chemotherapy – multi-agent
  - Capecitabine and oxaliplatin (called CAPOX)
  - 5-FU and leucovorin with oxaliplatin (FOLFOX)
  - 5-FU and leucovorin with irinotecan (FOLFIRI)
- Radiation Therapy – External Beam

SSDs for Hepatopancreatobiliary

- FCDS only Requires 1 SSDIs for these neoplasms – Fibrosis Score
- Fibrosis Score – liver and intrahepatic bile ducts
- Gallbladder – Schema Discriminator 1 – which staging criteria
  - Gallbladder (primary site C240 only)
  - Perihilar Bile Ducts
  - Distal Bile Ducts
- Stomach & Esophagus – Schema Discriminator 1
  - Location Relative to GE Junction
  - Undifferentiated Carcinoma, NOS
- CoC Required – NOT FCDS Required – SSDIs in addition to above:
  - Alpha-Fetoprotein – Value and Interpretation
  - Bilirubin – Value and Unit of Measure
  - Creatinine – Value and Unit of Measure
  - International Normalized Ratio for Prothrombin Time (PTT)
  - Primary Sclerosing Cholangitis
  - Tumor Growth Pattern
  - CA19-9 Value
Tumor Markers and Genetic Testing
Upper GI Tract (including biliary)

- CEA – not for upper GI Tract tumors – for lower GI Tract tumors
- CA19-9 – Pancreas, Gallbladder, Bile Duct, Stomach – blood – To assess whether treatment is working
- AFP – Liver – blood – To help diagnose liver cancer and follow response to treatment; to assess stage, prognosis, and response to treatment of germ cell tumors
- C-kit/CD117 – GIST – tissue, blood, bone marrow – To help in diagnosing and determining treatment
- Chromogranin A (CgA) – neuroendocrine tumors – blood – To help in diagnosis, assessment of treatment response, and evaluation of recurrence
- Des-gamma-carboxy prothrombin (DCP) – Hepatocellular – blood – To monitor effectiveness of treatment and detect recurrence
- DPD gene mutation – Pancreas, Stomach – tissue – To predict risk of toxic reaction to 5-fluorouracil therapy
- Gastrin – Gastrinoma – blood – To help in diagnosis, to monitor effectiveness of treatment, to detect recurrence
- HER2/neu gene amplification or protein overexpression – pancreas, stomach – tissue – pancreas, stomach – tissue – To determine whether treatment with certain targeted therapies is appropriate
- 5-HIAA – carcinoid tumors – urine – To help in diagnosis and to monitor disease
- Programmed death ligand 1 (PD-L1) – stomach, liver, ge junction – tissue – To determine whether treatment with a particular type of targeted therapy is appropriate
- Somatostatin receptor – neuroendocrine tumors affecting pancreas or GI Tract (GEP-NETs) – tissue – To determine whether treatment with a particular type of targeted therapy is appropriate
- Liquid Biopsy/Blood Test – assay testing hundreds of genetic mutations to define profile for this tumor
- FoundationOne® CDx (F1CDx) genomic test – see Jan 2021 FCDS Memo – any solid tumor – tissue – A companion diagnostic test to determine whether treatment with a particular type of targeted therapy is appropriate
- Guardan360 CDx genomic test – see Jan 2021 FCDS Memo – any solid tumor – tissue – A companion diagnostic test to determine whether treatment with a particular type of targeted therapy is appropriate
Tumor Markers and Genetic Testing
Upper GI Tract (including biliary)

- FoundationOne CDx - FoundationOne CDx is the first FDA-approved tissue-based broad companion diagnostic (CDx) that has been clinically and analytically validated for all solid tumors. Test results include microsatellite instability (MSI) and tumor mutational burden (TMB) to help inform immunotherapy decisions, and loss of heterozygosity (LOH) for ovarian cancer patients.

- You can also order PD-L1 immunohistochemistry (IHC) testing* as an optional add-on test. The FoundationOne CDx test detects substitution, insertion and deletion genetic alterations, and genetic copy number alterations (CNAs) in 324 genes and select gene rearrangements, as well as genomic signatures including microsatellite instability (MSI) and tumor mutational burden (TMB) using DNA isolated from formalin-fixed paraffin embedded (FFPE) tumor tissue specimens.

- FoundationOne CDx (324 DNA genes interrogated from a tissue sample)
- FoundationOne Liquid CDx (324 DNA genes* interrogated from a simple blood draw)
- FoundationOne Heme (406 DNA and 265 RNA genes interrogated from a variety of sample options)
Tumor Markers and Genetic Testing
Upper GI Tract (including biliary)

- Guardant360 CDx - Guardant360® CDx is a qualitative next generation sequencing-based in vitro diagnostic test that uses targeted high throughput hybridization-based capture technology for detection of single nucleotide variants (SNVs), insertions and deletions (indels) in 55 genes, copy number amplifications (CNAs) in two (2) genes, and fusions in four (4) genes. Guardant360 CDx utilizes circulating cell-free DNA (cfDNA) from plasma of peripheral whole blood collected in Streck Cell-Free DNA Blood Collection Tubes (BCTs).

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<th>Alteration Type</th>
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<td>Single Nucleotide Variants (SNVs)</td>
<td>AKTI, ALK, APC, AR, BRAF, ATM*, BRCAP110, BRCAP110**, CDH1, CDH3, CDH5, CDK4, CDKN2A, CDKN2B, CNOT1, CNOT3, CNOT4, CNOT5, CNOT6, CNOT7, CNOT8, CNOT9, CNOT10, CTNNB1, EGFR, ERBB2, ESR1, FGFR1, FGFR2, FGFR3, GATA4, GATA6, GNAS, HRAS, IDH1, IDH2, KRAS, MAP2K1, MAP2K2, MET, MLL1, MYC, MYD110, NF1, NFE2L2, NRAS, NTRK1, NTRK2, P38KRA, P38KRB, P38KRC, PTEN, RAL1, RET, BHER, ROS1, SMD4, SMO, STK11, TERT, TSC1, TSC2</td>
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<td>Indels</td>
<td>AKTI, ALK, APC, ATM*, BRCAP110, BRCAP110**, CDH1, CDH3, CDH5, CDK4, CDKN2A, CDKN2B, CNOT1, CNOT3, CNOT4, CNOT5, CNOT6, CNOT7, CNOT8, CNOT9, CNOT10, CTNNB1, EGFR, ERBB2, ESR1, FGFR1, FGFR2, FGFR3, GATA4, GATA6, GNAS, HRAS, IDH1, IDH2, KRAS, MAP2K1, MAP2K2, MET, MLL1, MYC, MYD110, NF1, NFE2L2, NRAS, NTRK1, NTRK2, P38KRA, P38KRB, P38KRC, PTEN, RAL1, RET, BHER, ROS1, SMD4, SMO, STK11, TERT, TSC1, TSC2</td>
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<td>ERBB2, MET</td>
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<tr>
<td>Fusions</td>
<td>ALK, NTRK1, RET, ROS1</td>
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2021 Changes

- Retire Flat File Format – will allow flat file submissions/data transmissions until 6/30/2021
- XML File Format – 7/1/2021 (tentative)/optional for submissions starting Jan 2021
- 2021 New Reportable Criteria – ALL GIST, ALL Thymoma, Evolving Melanoma
- 2021 Not Reportable Criteria – Need to remove NIFTP, EFVPTC, EVFPTC and other histologies from thyroid and review non-invasive histologies for pancreas – need to clarify removals
- Schema ID – changes to criteria and one new schema added
- 2021 Solid Tumors – 2 newly revised chapters (Melanoma/Other) and changes to all 8 other chapters
- Expecting to see GYN Solid Tumor Rules before September 2021 according to ETC Training Schedules
- Please participate in any 2021 Updates Webinars sponsored by NAACCR, FCDS, SEER, CoC
- FCDS will be sponsoring some webinars – but, other experts may do a better job of explaining
2021 Changes

2021 New Data Items Required
- Name-Birth Surname – Replaces Maiden Name which will be Retired
- Medicare Beneficiary ID
- Grade Post Therapy Clinical (yc)
- Gleason Pattern Clinical
- Gleason Pattern Pathological
- Gleason Score Clinical
- Gleason Score Pathological
- Gleason Tertiary Pattern

Changed Data Items
- HER2 Overall Summary added to Esophagus and Stomach Schemas 00161, 00169, 00170
- Radiation Modality New Codes
- Changes to SSDIs
- FIGO Stage
- Grade – schema specific

Grade Field Conversions
Stage Conversions
SSDI Conversions
2021 Retired Data Items – TNM 6 & 7, Maiden Name
2021 FCDS DAM Revision
FCDSv21 EDITS Metafile
FCDSv21 Updates to Abductor Code Test & Review of Existing Q&A
2021 Grade Manual
2021 SSDI Manual
2021 Heme Updates
2021 Solid Tumors – 2 newly revised chapters (Melanoma/Other) and changes to all 8 other chapters
Expecting to see GYN Solid Tumor Rules before September 2021 according to ETC Training Schedules
2021 ICD-O-3 Updates
2021 STORE Manual

Resources
- American Cancer Society Introduction to Cancer Series By Cancer Site/Type – www.cancer.org
- NCCN Guidelines Series by Cancer Site/Type – www.nccn.org
- Cancers in Series from NCI, ACS and NCCN Include:
  - Esophagus
  - Stomach
  - Pancreas
  - Liver
  - Bile Duct
  - Gallbladder
  - Small Bowel
  - Mayo Clinic Website/Johns Hopkins Website/MD Anderson Website
  - Role of endoscopic ultrasound in the diagnosis of pancreatic cancer Juana Gonzalo-Marín, Juan José Vila, and Manuel Pérez-Miranda
- FoundationOne CDx and Guardian360 CDx Websites
Questions ......