Pancreatic Cancer

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THE UNIVERSITY OF TEXAS
MD Anderson Cancer Center
Making Cancer History®

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Objectives

- Define evaluation and diagnosis of pancreatic adenocarcinoma, and determine criteria for curative resection
- Define management guidelines for pancreatic adenocarcinoma including treatment modalities, surveillance, survivorship care
- Examine the NP role and multidisciplinary collaboration in the care of the pancreatic adenocarcinoma patient, then apply information presented through the use of case studies

Case Study I

Pancreatic Cancer

Third leading cause of cancer deaths in the US

Frequently a systemic disease at presentation

American Cancer Society 2024 estimates:

- **About 66,440 new cases**
  - 34,530 men
  - 31,910 women

- **About 51,750 people deaths**
  - 27,270 men
  - 24,480 women

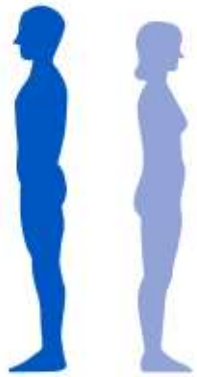
American Cancer Society 2024

Leading Sites of New Cancer Cases and Deaths – 2024 Estimates

American Cancer Society

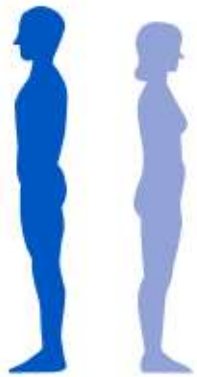
Estimated New Cases

Male			Female		
Prostate	299,010	29%	Breast	310,720	32%
Lung & bronchus	116,310	11%	Lung & bronchus	118,270	12%
Colon & rectum	81,540	8%	Colon & rectum	71,270	7%
Urinary bladder	63,070	6%	Uterine corpus	67,880	7%
Melanoma of the skin	59,170	6%	Melanoma of the skin	41,470	4%
Kidney & renal pelvis	52,380	5%	Non-Hodgkin lymphoma	36,030	4%
Non-Hodgkin lymphoma	44,590	4%	Pancreas	31,910	3%
Oral cavity & pharynx	41,510	4%	Thyroid	31,520	3%
Leukemia	36,450	4%	Kidney & renal pelvis	29,230	3%
Pancreas	34,530	3%	Leukemia	26,320	3%
All sites	**1,029,080**		**All sites**	**972,060**	



Estimated Deaths

Male			Female		
Lung & bronchus	65,790	20%	Lung & bronchus	59,280	21%
Prostate	35,250	11%	Breast	42,250	15%
Colon & rectum	28,700	9%	Pancreas	24,480	8%
Pancreas	27,270	8%	Colon & rectum	24,310	8%
Liver & intrahepatic bile duct	19,120	6%	Uterine corpus	13,250	5%
Leukemia	13,640	4%	Ovary	12,740	4%
Esophagus	12,880	4%	Liver & intrahepatic bile duct	10,720	4%
Urinary bladder	12,290	4%	Leukemia	10,030	3%
Non-Hodgkin lymphoma	11,780	4%	Non-Hodgkin lymphoma	8,360	3%
Brain & other nervous system	10,690	3%	Brain & other nervous system	8,070	3%
All sites	**322,800**		**All sites**	**288,920**	



Estimates are rounded to the nearest 10, and cases exclude basal cell and squamous cell skin cancers and in situ carcinoma except urinary bladder. Estimates do not include Puerto Rico or other US territories. Ranking is based on modeled projections and may differ from the most recent observed data.

Pancreatic Adenocarcinoma

- Overall 5-year survival rate low at 13%
- High frequency of subclinical metastases at initial presentation
- Systemic disease (extra-pancreatic involvement) generally precludes curative therapy
- Undetectable extra-pancreatic disease at the time of surgical resection contributes to recurrence

Cancer Statistics 2024

American Cancer Society

Trends in five-year relative survival (%), US, 1975–2019

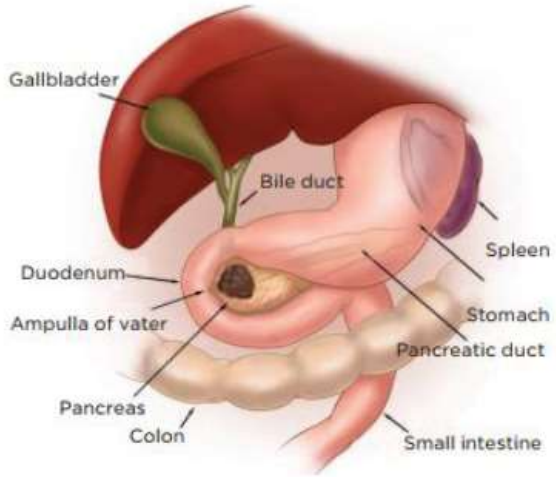
Site	1975-77	1995-97	2013-2019
All sites	49	63	69
Breast (female)	75	87	91
Colon & rectum	50	61	64
Leukemia	34	48	67
Liver & intrahepatic bile duct	3	7	22
Lung & bronchus	12	15	25
Melanoma of the skin	82	91	94
Non-Hodgkin lymphoma	47	56	74
Ovary	36	43	51
Pancreas	3	4	13
Prostate	68	97	97
Uterine cervix	69	73	67
Uterine corpus	87	84	81

Survival is age adjusted for normal life expectancy and are based on cases diagnosed in the Surveillance, Epidemiology, and End Results (SEER) 9 areas for 1975-1977 and 1995-1997 and in the SEER 22 areas for 2013-2019; all cases were followed through 2019.
Source: Surveillance, Epidemiology, and End Results program, National Cancer Institute, 2023.

Pancreas

Mainly contains two kinds of cells:

- Exocrine cells – produces digestive enzymes
- Endocrine cells – produces hormones directly into the bloodstream



Majority (~95%) of pancreatic malignancies arise from exocrine cells

Types of Pancreatic Cancer

2 Most Common Types

- Adenocarcinoma (85%) – exocrine/ductal cell origin
- Neuroendocrine (< 5%) - endocrine/islet cell origin

Other Types:

- Adenosquamous carcinoma
- Acinar cell carcinomas
- Signet ring cell carcinoma
- Squamous cell carcinoma
- Undifferentiated carcinoma

Pancreatic Adenocarcinoma

- Most common pancreatic malignancy
- Arises from exocrine cells
- Commonly referred to as pancreatic cancer

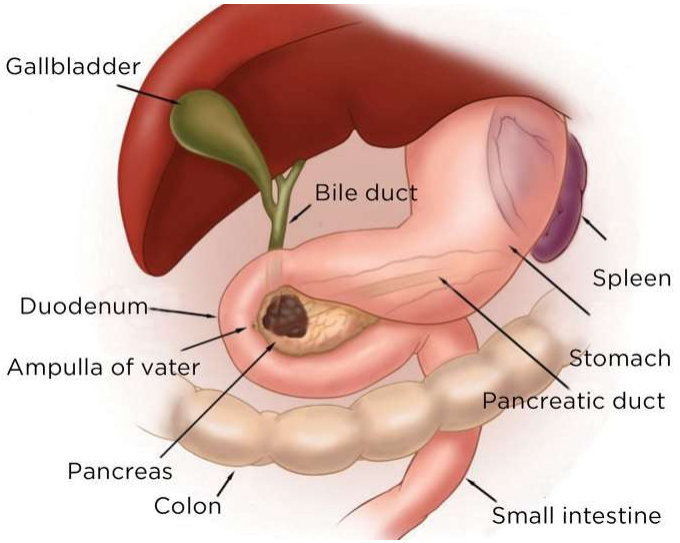
Will be the focus of this presentation

Risk Factors

- Smoking
- Diabetes
- Obesity
- Heavy alcohol consumption
- Chronic Pancreatitis
- Family History of pancreatic cancer
- Inherited Mutations
  - (ex: BRCA mutations, CDKN2A, PALB, ATM, MLH1, MSH2, MSH6, etc)
- Genetic Syndromes (Lynch Syndrome)

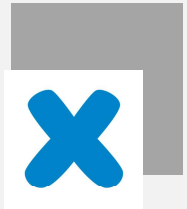
Common Presenting Signs & Symptoms

- Jaundice from biliary obstruction
- Manifestations depend on tumor location
- Generally non-specific but could include:
  - Weight loss
  - Steatorrhea
  - Abdominal pain (radiates to the back)
  - Recent DM diagnosis
  - Nausea
  - Cachexia w/ advanced disease
  - Ascites w/ advanced disease

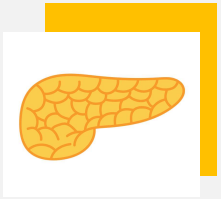


Is there a role for screening for pancreatic adenocarcinoma in the general population?

No established standard for screening or prevention for general population

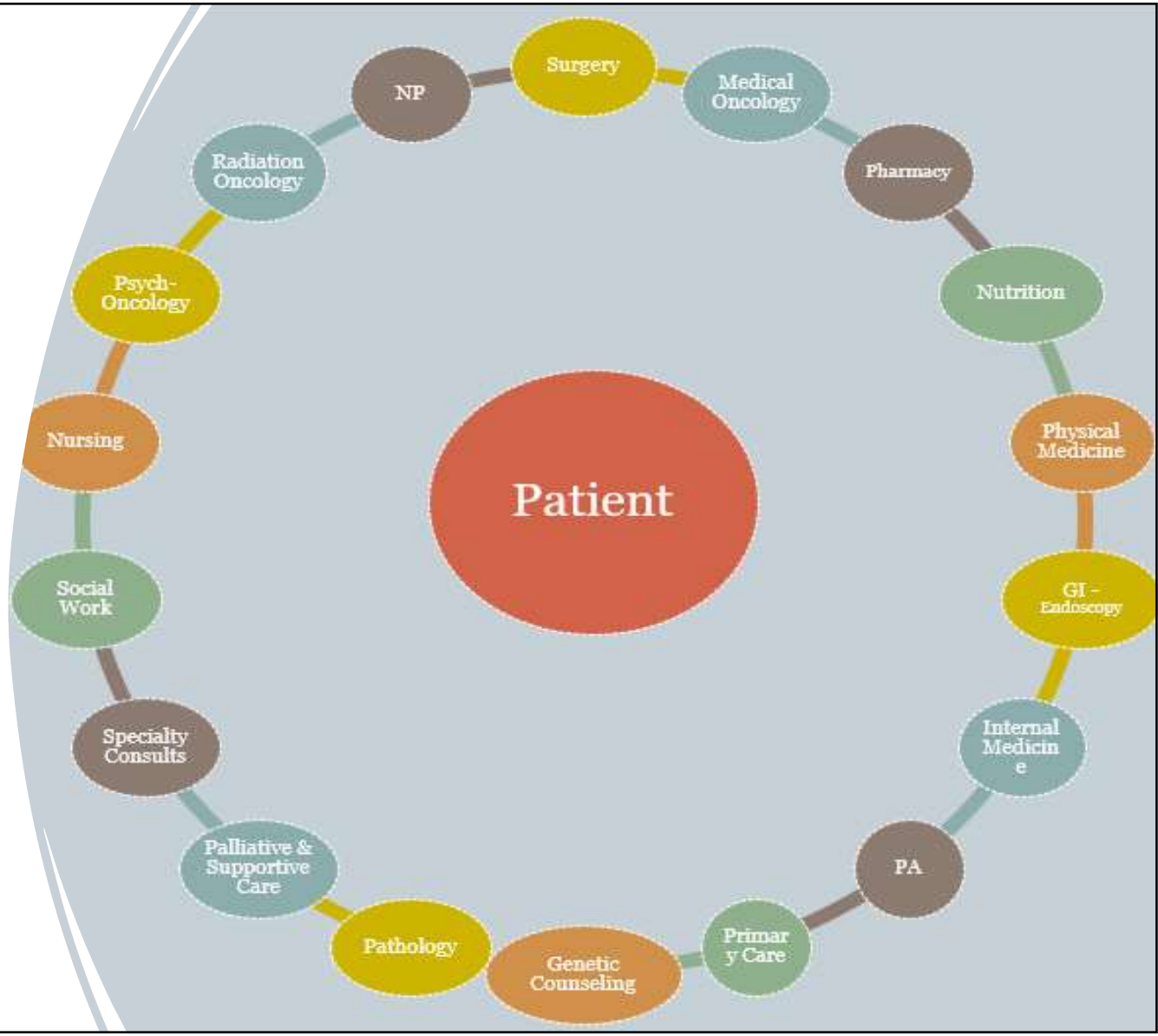


No single reliable test for early detection of pancreatic cancer for the general population



Imaging or endoscopic studies may be considered for patients with genetic predisposition

Multidisciplinary Collaboration is Essential!



Diagnostic Evaluation

Primary Goals

1. Establish tissue diagnosis
2. Determine disease stage and eligibility for tumor resection

Lab Evaluation

1. CA19-9
   - Can have clinical value as tumor marker
   - May be elevated during cholestasis
   - Some patients do not express elevations and may have low/undetectable levels despite advanced disease
2. CBC
   - Check for anemia
   - Check for indication of biliary-related infection
3. CMP, A1C, Enzymes
   - Check liver function and indication of obstruction
   - Blood sugar elevations
   - Pancreatitis

Diagnostic Imaging

CT SCAN
- Pancreas Protocol
- Multiphase, Helical, W/ Contrast

MRI

PET SCAN

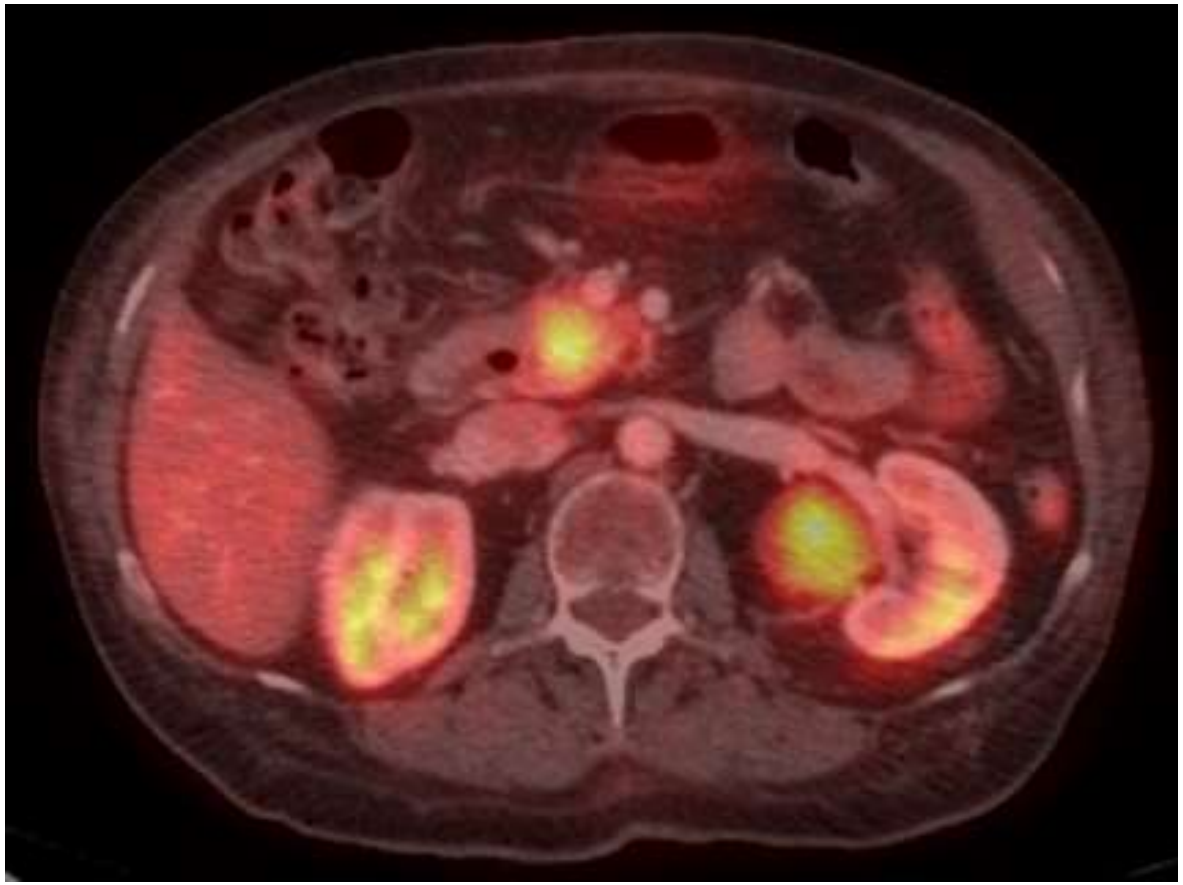
Diagnostic Evaluation

Primary pancreatic tumor

Diagnostic Evaluation

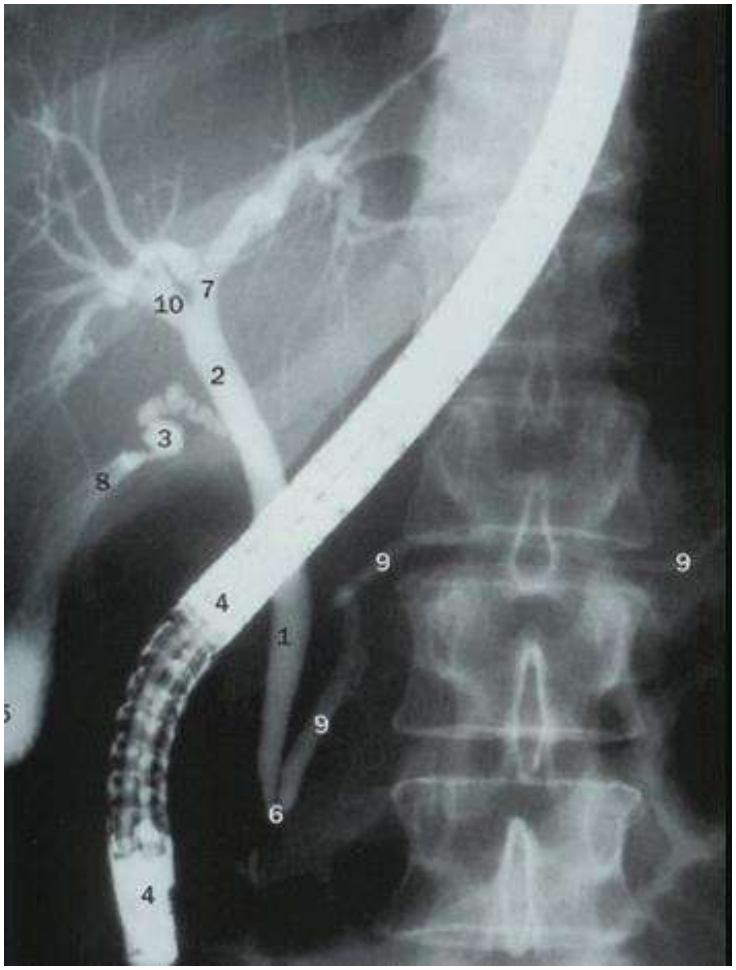
Liver Metastases

Diagnostic Imaging



ERCP:

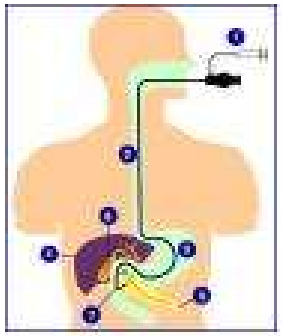
- Therapeutic (stent placement to relieve biliary obstruction)
- Diagnostic (evaluate stricture and obtain brushings for cytologic testing)



Stent for Biliary Decompression

Endoscopic Ultrasound

- Performed with FNA for biopsy



Evaluation: Biopsy

- ERCP brushings
- EUS with Fine Needle Aspiration of Primary Tumor
- Imaging-guided FNA/Biopsy (helpful for biopsy confirmation of metastasis)

Evaluation

- Diagnostic Laparoscopy
- Surgery

Additional Tests

- Genetic testing for inherited mutations
- Molecular profiling of tumor tissue

American Joint Committee on Cancer 8th Edition Staging System for Pancreatic Cancer.

T	Primary Tumor	N	Number of Regional PLNs	Stage	T	N	M
T1	≤2 cm	N0	0	IA	1	0	0
T2	>2 cm, ≤4 cm	N1	1 to 3	IB	2	0	0
T3	>4 cm	N2	≥4	IIA	3	0	0
T4	CA, SMA, and/or CHA invasion			IIB	1–3	1	0
				III	4	Any	0
					Any	2	
				IV	Any	Any	1

Abbreviations: PLN—positive lymph node; CA—celiac axis; SMA—superior mesenteric artery; CHA—common hepatic artery.

Kang, et al 2022 doi: 10.3390/cancers14194672. PMID: 36230595; PMCID: PMC9563770.

Resectability/Radiographic Staging of Pancreatic Cancer

Vascular Structures That Determine Stage of Disease for Localized Pancreatic Cancer	Resectable	Borderline Resectable	Locally Advanced	
			Type A	Type B
Tumor-artery anatomy				
SMA (usually pertains to tumor of head or uncinate process)	No radiographic evidence of abutment or encasement	≤ 180° (abutment)	> 180° (encasement) but ≤ 270°	> 270° encasement
Celiac artery (usually pertains to tumor of pancreatic body)	No radiographic evidence of abutment or encasement	≤ 180° (abutment)	> 180° (encasement) but does not extend to aorta and amenable to celiac resection (with or without reconstruction)	> 180° and abutment/ encasement of aorta
Hepatic artery (usually pertains to tumor of pancreatic neck/head)	No radiographic evidence of abutment or encasement	Short-segment abutment/encasement without extension to celiac artery or hepatic artery bifurcation	> 180° encasement with extension to celiac artery and amenable to vascular reconstruction	> 180° encasement with extension beyond bifurcation of proper hepatic artery into right and left hepatic arteries
Tumor-vein anatomy				
SMV-PV	≤ 50% narrowing of SMV, PV, SMV-PV	> 50% narrowing of SMV, PV, SMV-PV **with** distal and proximal target for reconstruction	Occlusion **without** obvious option for reconstruction	
Traditionally considered for resection after neoadjuvant therapy	Yes	Yes	No	No

Abbreviations: PV, portal vein; SMA, superior mesenteric artery; SMV, superior mesenteric vein; SMV-PV, superior mesenteric-portal vein.

Source: Evans (2018) ASCO Educational Book. Volume 38. https://doi.org/10.1200/EDBK_200861

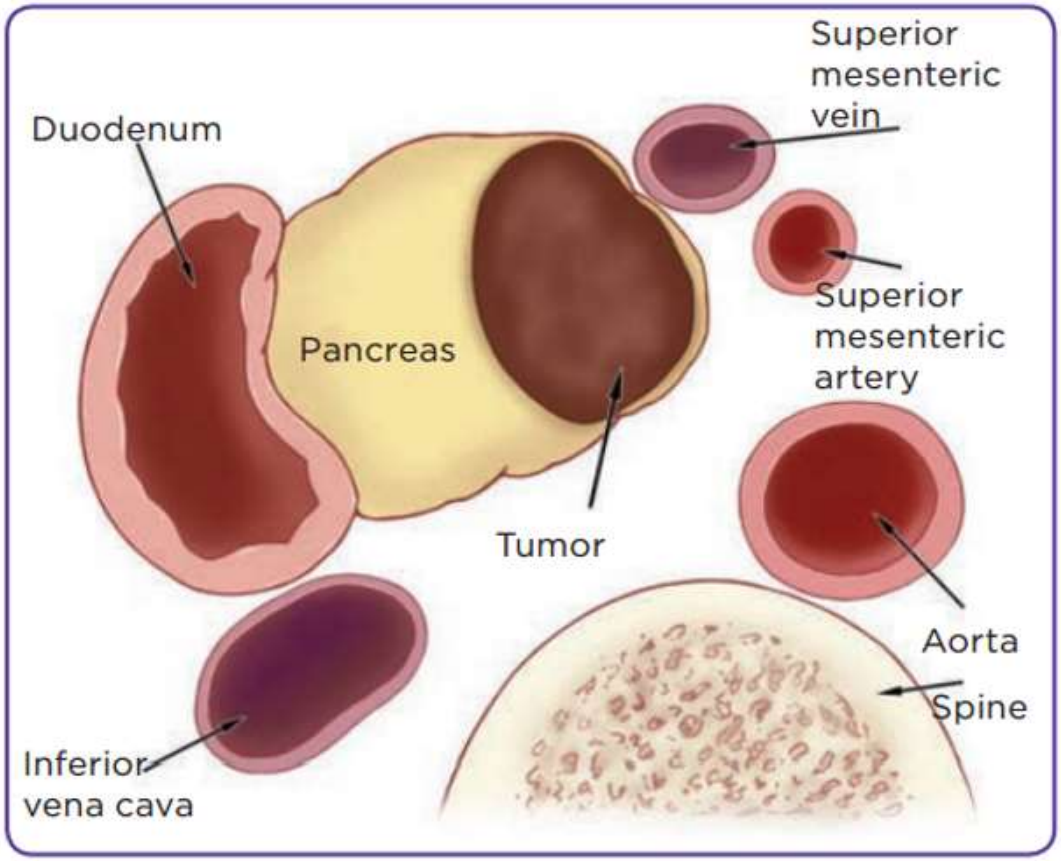
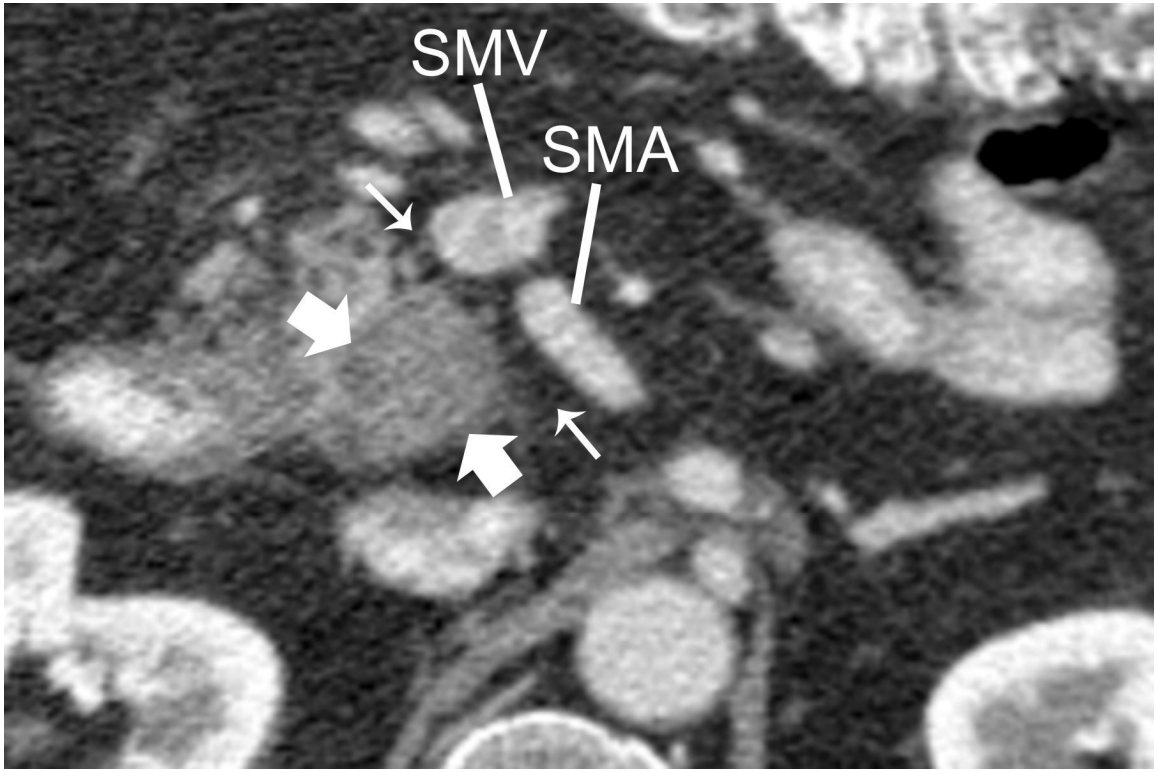
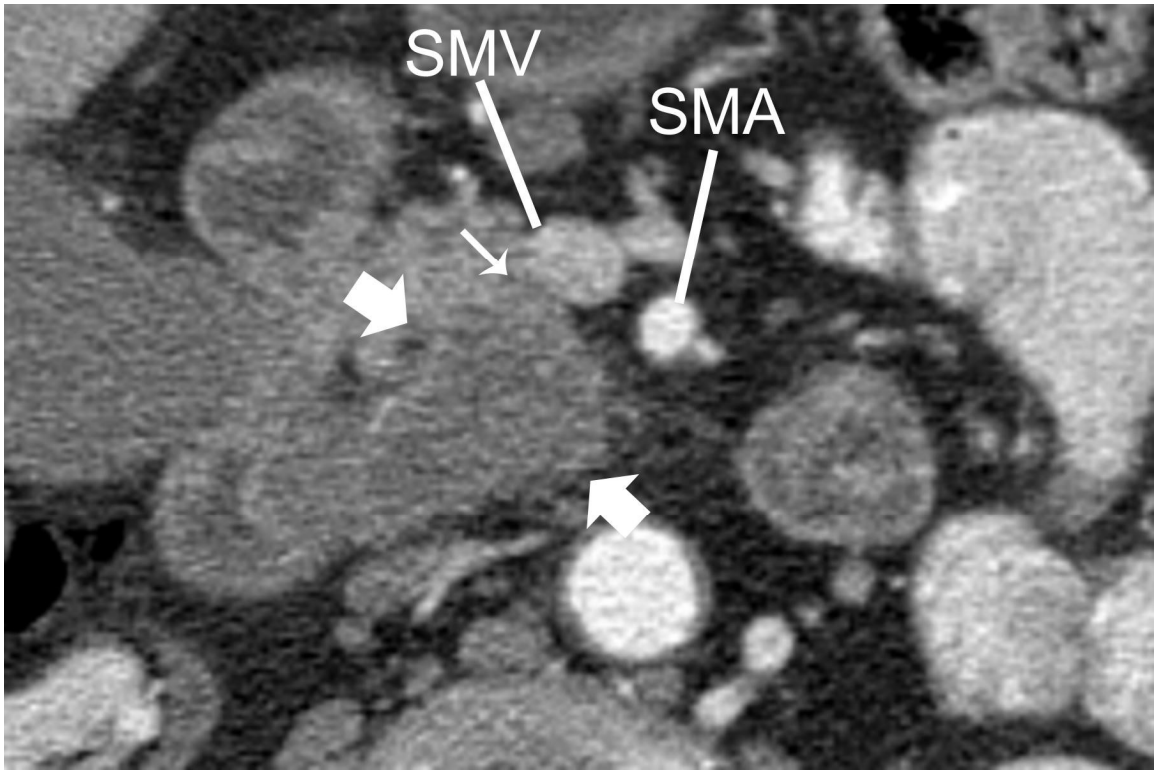


Figure 2. Resectable pancreatic cancer. ©2008 The University of Texas MD Anderson Cancer Center.


SMV
SMA


SMV
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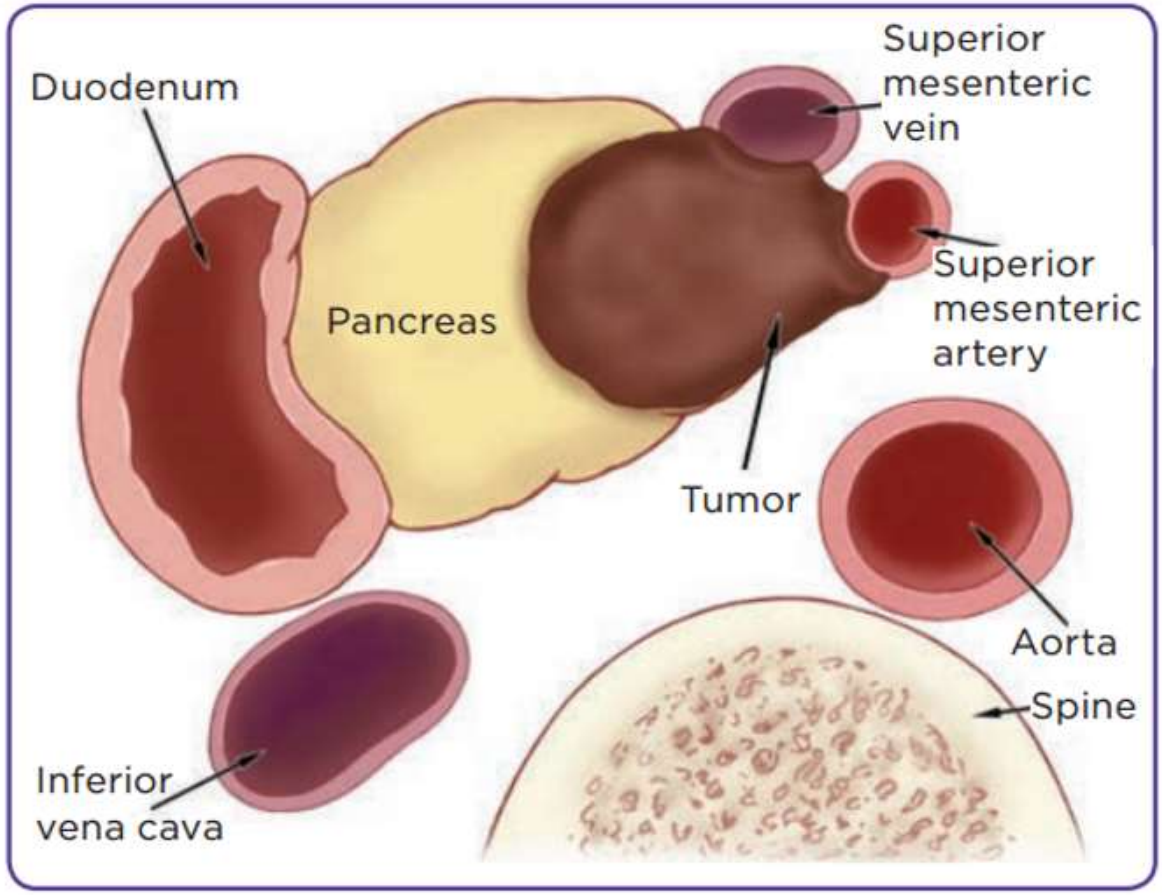
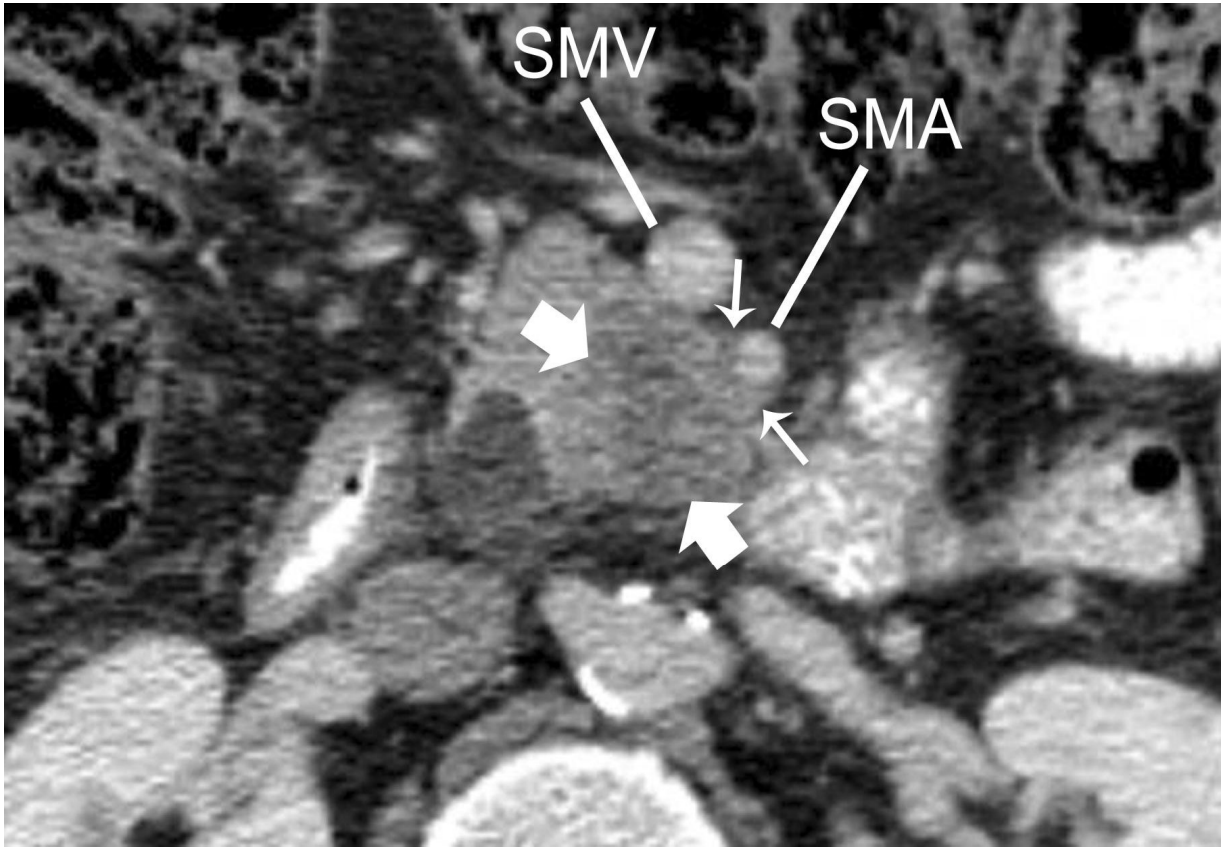


Figure 3. Borderline resectable pancreatic cancer. ©2008 The University of Texas MD Anderson Cancer Center.


SMV
SMA

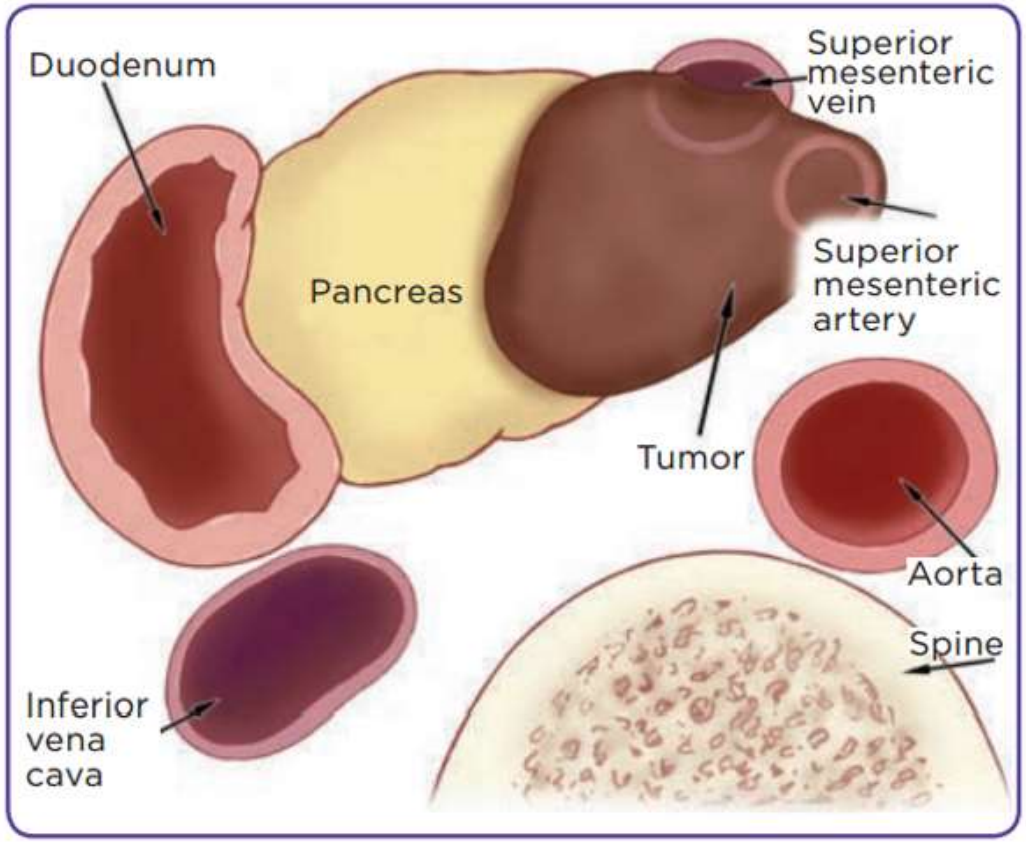
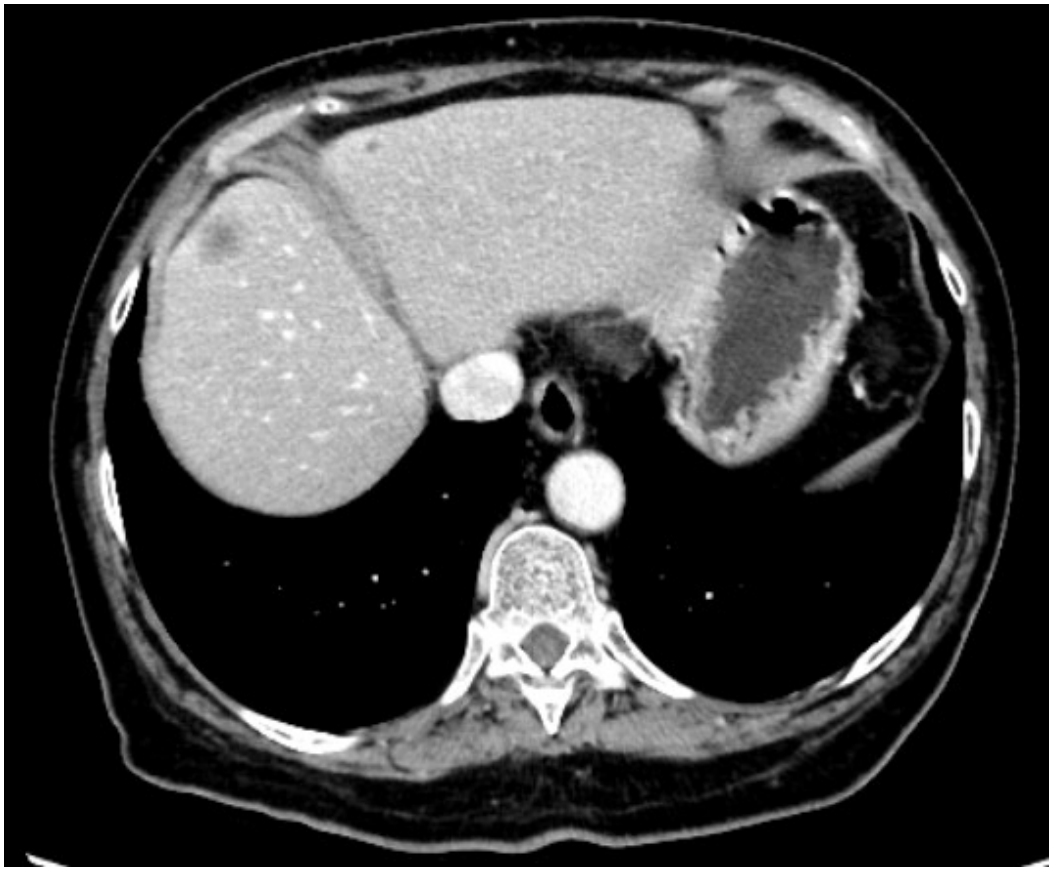


Figure 4. Locally advanced pancreatic cancer. ©2008 The University of Texas MD Anderson Cancer Center.



Case Study II

Treatment Modalities

Surgery
- The sole potentially-curative treatment for pancreatic cancer
- Type of surgery will depend on tumor location
- Diagnostic laparoscopy for some patients

Systemic Therapy
- Adjuvant vs. neo-adjuvant approach
- Genetic/molecular testing can help with determining most appropriate regimen

Radiation
- Different types and dosing/fractionation

NCCN offers evaluation and treatment guidelines

Surgery

Pancreaticoduodenectomy (Whipple Procedure)

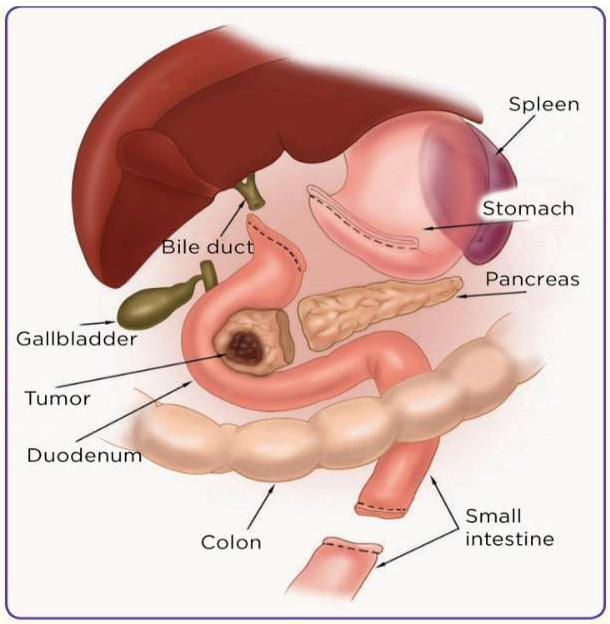


Figure 5

Pancreaticoduodenectomy: resection of distal stomach, bile duct, gallbladder, duodenum, head of the pancreas. ©2008 The University of Texas MD Anderson Cancer Center.

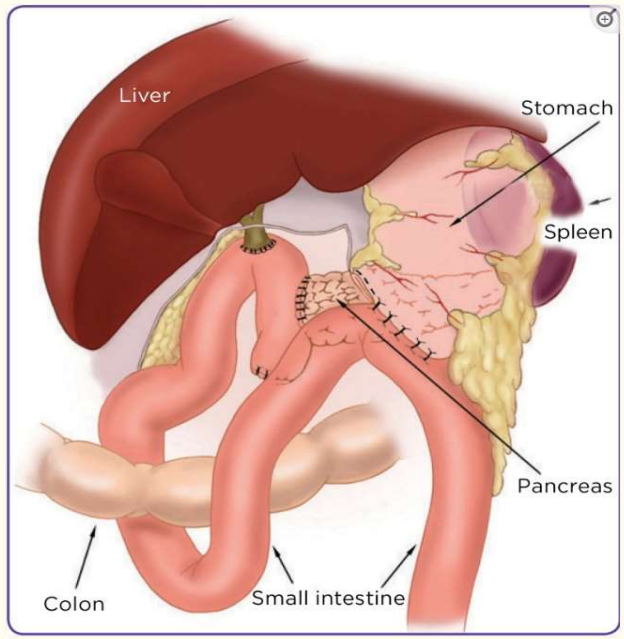


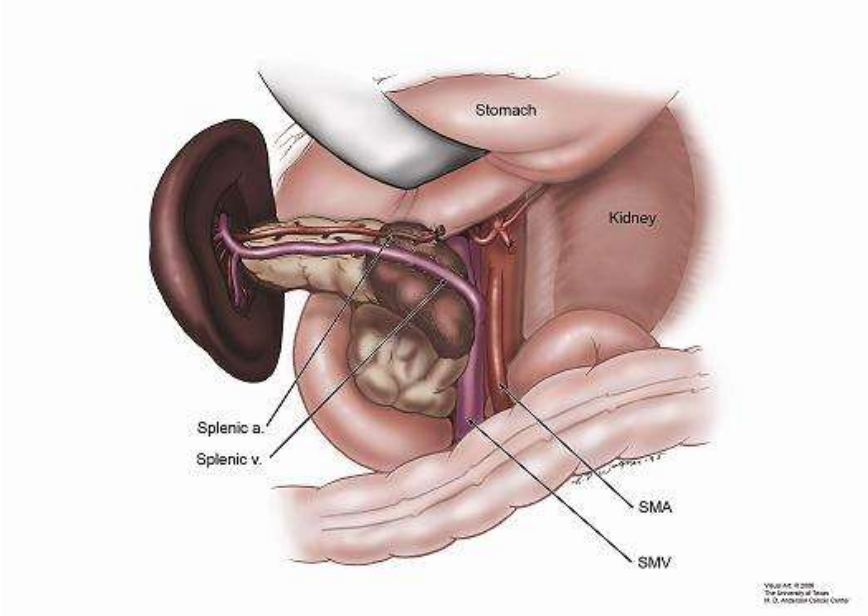
Figure 6

Pancreaticoduodenectomy: postresection anastomoses. ©2008 The University of Texas MD Anderson Cancer Center.

Surgery
Distal Pancreatectomy

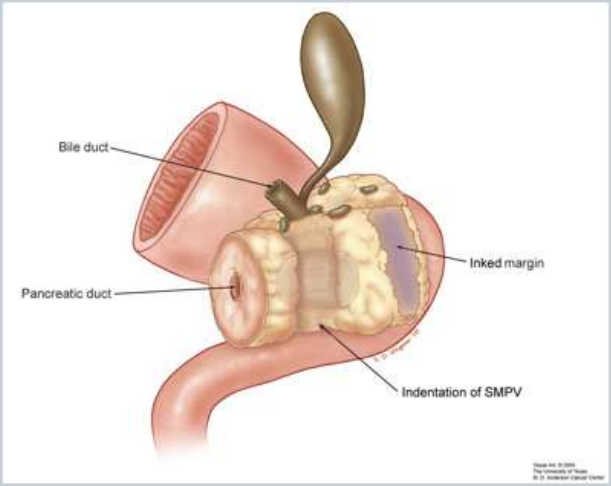
Patient will require vaccination if performed with splenectomy:

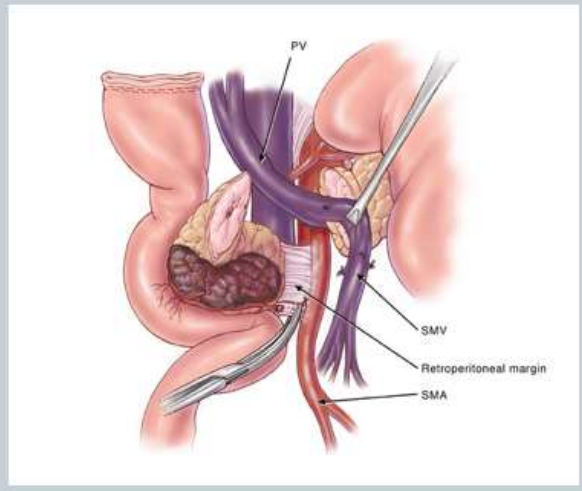
- Meningococcal
- Pneumococcal
- Haemophilus B



Resection Margin

- R0 – resection margin negative
- R1 – resection margin microscopically positive
- R2 - resection margin positive



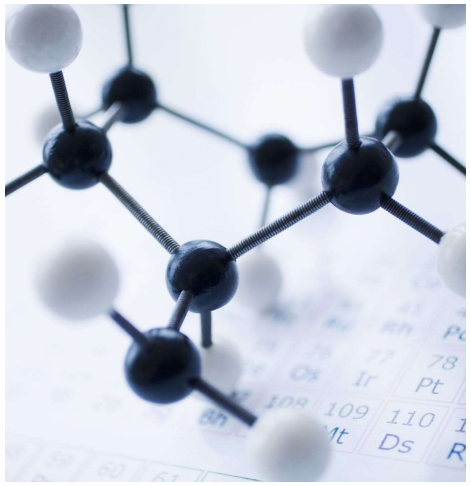


Post-op Care

- Potential Complications
  - Abscess/Infection
  - Delayed gastric emptying
  - Anastomosis leak
  - GI Bleeding
  - Colitis
  - Ileus
  - Pneumonia
- Nutrition management and support is essential
- Post-Op medications
  - Pancreatic Enzymes
  - Anti-ulcer Therapy

Common Chemotherapy Agents

- FOLFIRINOX
  - Folinic acid
  - Fluorouracil
  - IRINotecan
  - OXaliplatin
- Gemcitabine + NAB-paclitaxel
- Capecitabine
  - also used as radiosensitizer
- Gemcitabine + Cisplatin
  - Consider for BRCA, PALB2 mutations



Genetic/molecular testing can help with determining most appropriate regimen

Side Effects

Side effect profile may vary between chemotherapeutic agents

Could Include:

- Fatigue
- Peripheral Neuropathy
- Diarrhea
- Nausea
- Anemia, CBC abnormal values

Immunotherapy

- Pembrolizumab
- Dostarlimab--gxly
  - Targets checkpoint proteins on immune system cells that helps keep T cells from attacking normal cells after destroying “invaders”. Immunotherapy can “suppress the brakes” and boosts immune response against cancer cells.
  - Can be used for unresectable disease, metastasis, or recurrence
  - Can be options for patients who have tested positive for specific gene changes: high level of microsatellite instability (MSI-H)
    - ✓changes in one of the mismatch repair (MMR) genes
    - ✓tumors found to have a high tumor mutation burden (TMB-H)

Immunotherapy Side Effects

Fatigue

Fever

Headaches

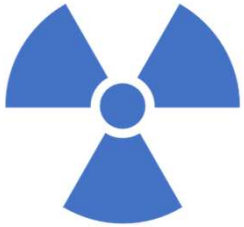
Inflammatory response

- Pneumonitis
- Colitis
- Hypophysitis
- Rash
- Skin pigment changes

Radiation

Delivery:

- Conventional External Beam Therapy
- Stereotactic body radiation Therapy (SBRT)
- Intensity-modulated Radiation Therapy (IMRT)



Considerations:

- Neo-adjuvant – may increase likelihood of margin-negative resection if administered before surgical resection (neo-adjuvant)
- Adjuvant – given after resection based on patient clinical status and disease stage/pathology/risks
- Palliative – for symptom control

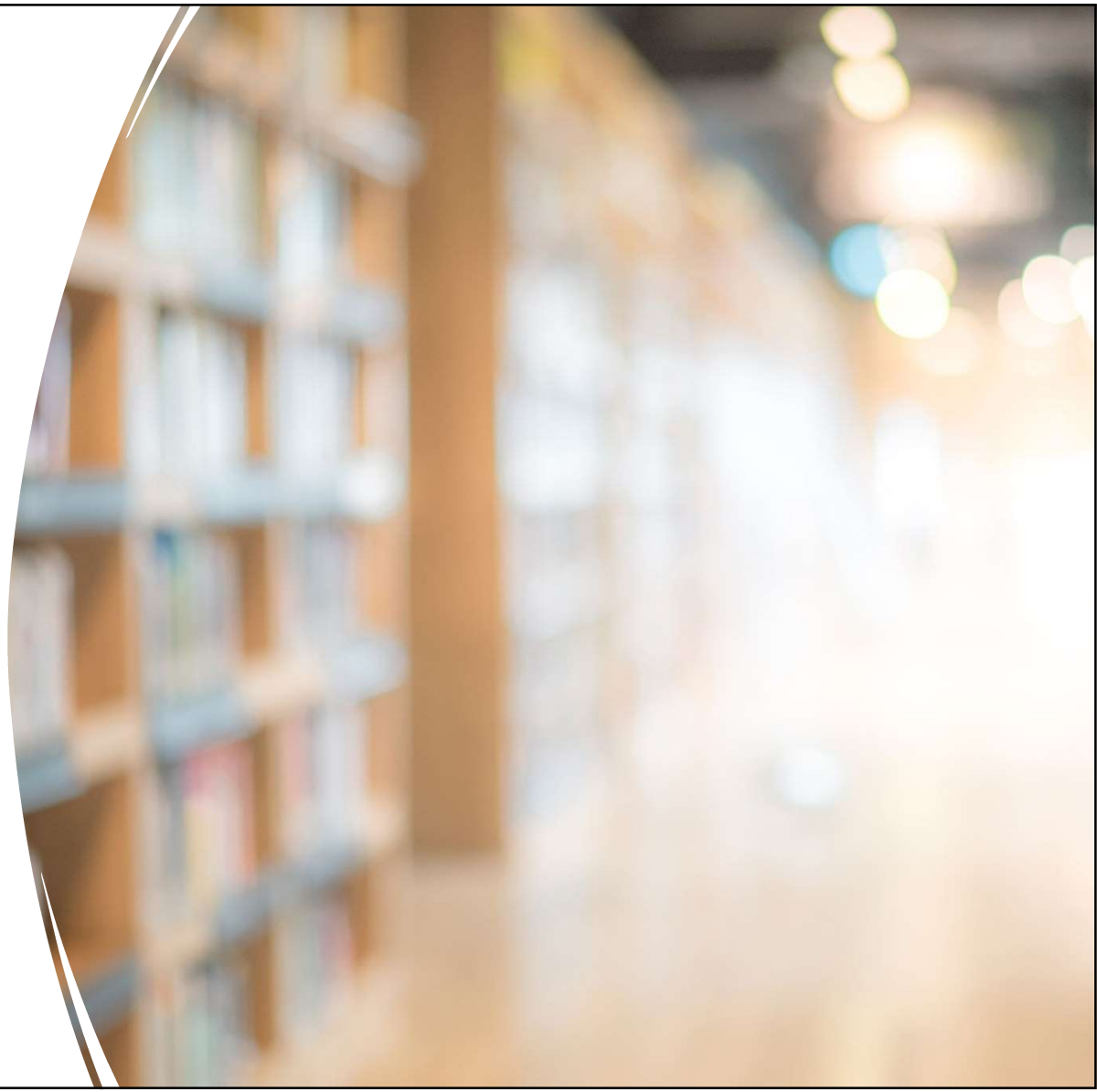
Advances and Future Direction

- Targeted Therapy
- Vaccine Therapy

Survivorship

- Continue Imaging and Labs
- Long-Term Nutrition Management
- Evaluate and Manage Micronutrient Deficiencies
- Evaluate for Potential Long-Term Sequalae of Oncologic Therapy
  - Bone Health
  - Risk for Diabetes
- Formal Survivorship Care Program/Clinic
- Critical to coordinate care with Primary Care Providers

Case Study III



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