

Neoplasms of the Exocrine Pancreas

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Epidemiology and Risk Factors

- 265,000 people annually
- 74% of patients die within the first year after diagnosis
- The worst prognosis of all malignancies with a 5-year survival rate of only 6%

Epidemiology and Risk Factors

- Complex interaction of genetic and environmental factors
- Most patients >60 years old
- Slightly more common in men than women
- **Risk factors**
 - Smoking twofold₁
 - Diets high in fat and low in fiber
 - Diabetes₂
 - Chronic pancreatitis, especially familial pancreatitis₃

1. Gold EB, Goldin SB: Epidemiology of and risk factors for pancreatic cancer. Surg Oncol Clin N Am. 1998;7:67

2. Jean M, Lowy A, Chiao P et al.: The Molecular Biology of Pancreatic Cancer. New York: Springer-Verlag; 2002

3. Lowenfels AB, Maisonneuve P, Whitcomb DC. Risk factors for cancer in hereditary pancreatitis. International Hereditary Pancreatitis Study Group. Med Clin North Am. 2000;84:565–575.

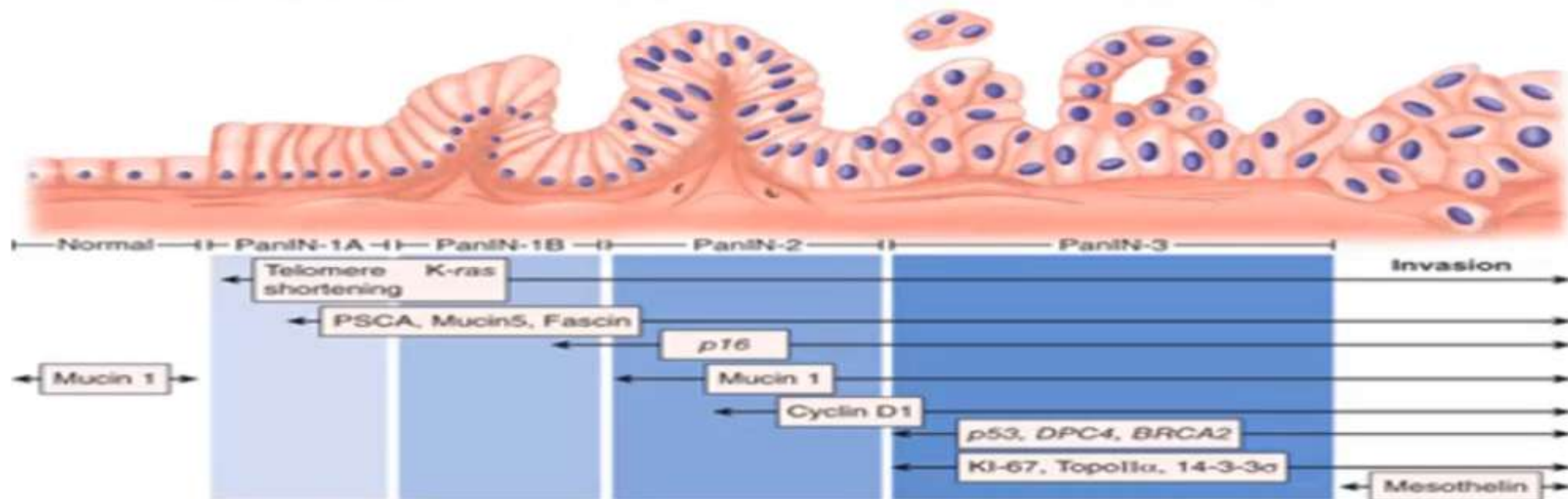
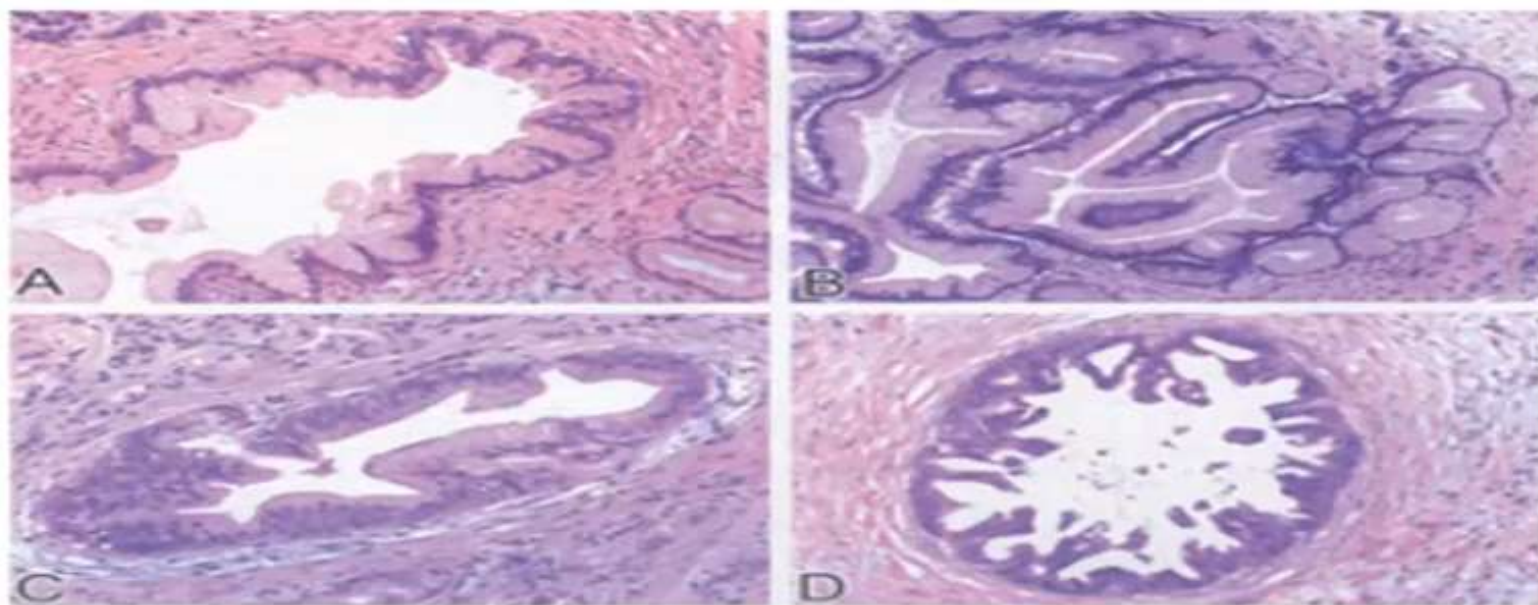
Genetics of Pancreatic Cancer

- 10% has inherited genetic predisposition.
- Family history of pancreatic cancer in a first-degree relative has twofold increased risk
- The K-ras oncogene 90%¹
- The HER-2/neu oncogene²
- Multiple tumor-suppressor genes are deleted and/or mutated in pancreatic cancer
 - p53
 - p16
 - DPC4 (Smad 4)
 - BRCA2¹
- Most pancreatic cancers have three or more of the above mutations

1. Berger D, Fischer W. Inherited Pancreatic Cancer Syndromes. New York: Springer-Verlag; 2002

2. Jean M, Lowy A, Chiao P et al.: The Molecular Biology of Pancreatic Cancer. New York: Springer-Verlag; 2002

Pathology



Pathology

- **Location**

- 65% Head or unciniate process
- 15% The body
- 10% The tail
- Diffuse involvement of the gland

Pathology

- **Histologic Types**

- Ductal adenocarcinoma 75%
- Adenosquamous carcinoma
- Acinar cell carcinoma

Diagnosis and Staging

- **Tumor (T)**

- TX: Primary tumor cannot be assessed
- T0: No evidence of primary tumor
- Tis: Carcinoma in situ
- T1: Tumor is limited to the pancreas and is ≤ 2 cm in greatest dimension
- T2: Tumor is limited to the pancreas and is >2 cm in greatest dimension
- T3: Tumor extends beyond the pancreas but without involvement of the celiac axis or the superior mesenteric artery
- T4: Tumor involves the celiac axis or the superior mesenteric artery (unresectable primary tumor)

Diagnosis and Staging

- **Regional lymph nodes (N)**
 - NX: Regional lymph nodes cannot be assessed
 - N0: No regional lymph node metastasis
 - N1: Regional lymph node metastasis

- **Distant metastasis (M)**
 - MX: Distant metastasis cannot be assessed
 - M0: No distant metastasis
 - M1: Distant metastasis

Diagnosis and Staging

Stage	T	N	M	Description
IA	1	0	0	Limited to pancreas ≤ 2 cm
IB	2	0	0	Limited to pancreas > 2 cm
IIA	3	0	0	Extends beyond pancreas but does not involve arteries
IIB	1-3	1	0	Any tumor without artery involvement with lymph node involvement
III	4	Any	0	Tumor involves arteries (unresectable)
IV	Any	Any	1	Any tumor with distant metastases

Diagnosis and Staging

- **8%** localized stage
- **27%** spread to regional lymph nodes or directly beyond the primary site
- **53%** metastasized (distant stage)
- **The corresponding 5-year relative survival rates**
 - **23.3%** for localized
 - **8.9%** for regional
 - **1.8%** for distant
- The overall 5-year relative survival rate **5.8%**¹

Howlader N, Noone AM, Krapcho M et al. SEER Cancer statistics review 1975-2009 (Vintage 2009 populations) National Cancer Institute, Bethesda. Available at: http://seer.cancer.gov/csr/1975_2009_pops09/.

Diagnosis

- Lack of tools for early diagnosis
- The majority of patients present with pain and jaundice
- **On physical examination**
 - Weight loss
 - Skin is icteric
 - Palpable distended gallbladder 25% of patients
- More fortunate patients have tumors situated such that biliary obstruction and jaundice occurs early and prompts diagnostic tests

Diagnosis

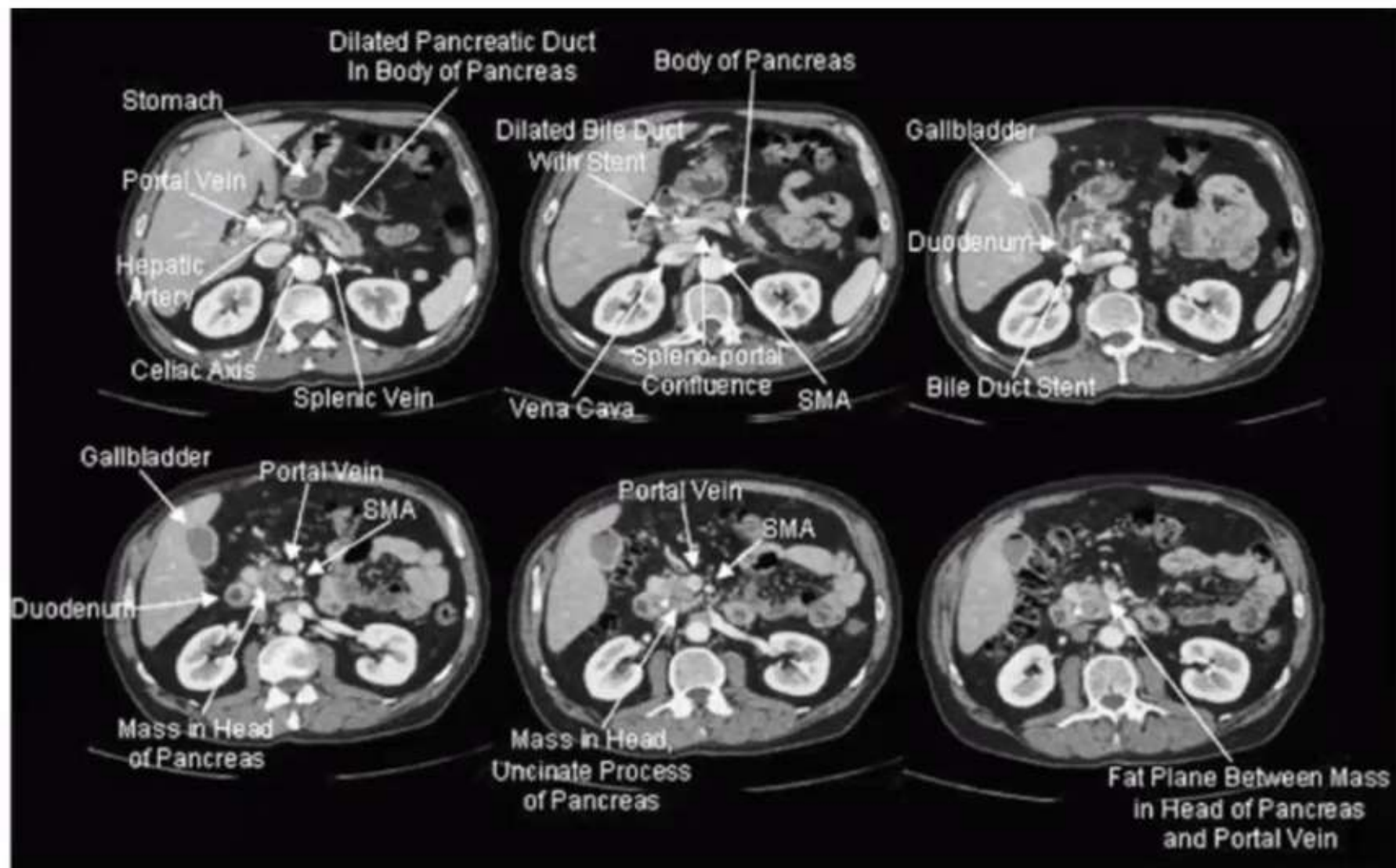
- A low threshold for ordering a CT scan with “pancreatic protocol” elderly patients with unexplained, persistent, although vague, abdominal pain.
- New-onset diabetes in an elderly patient, especially if combined with vague abdominal pain
- CA19-9 are elevated in about 75% of patients with pancreatic cancer. However, CA19-9 is also elevated in about 10% of patients with benign diseases of the pancreas, liver, and bile ducts.

Diagnosis

- In patients presenting with jaundice
- **Abdominal ultrasound**
 - bile duct dilation with absence of stones
- **CT scan**
 - Detect the tumor
 - Asses resectability
 - Liver metastasis

CT scan

- **CT findings that indicate a tumor is unresectable**
 - Involvement of ≥ 180 degrees of the celiac axis, hepatic or superior mesenteric artery
 - Enlarged lymph nodes outside the boundaries of resection
 - Ascites
 - Distant metastases (e.g., liver).

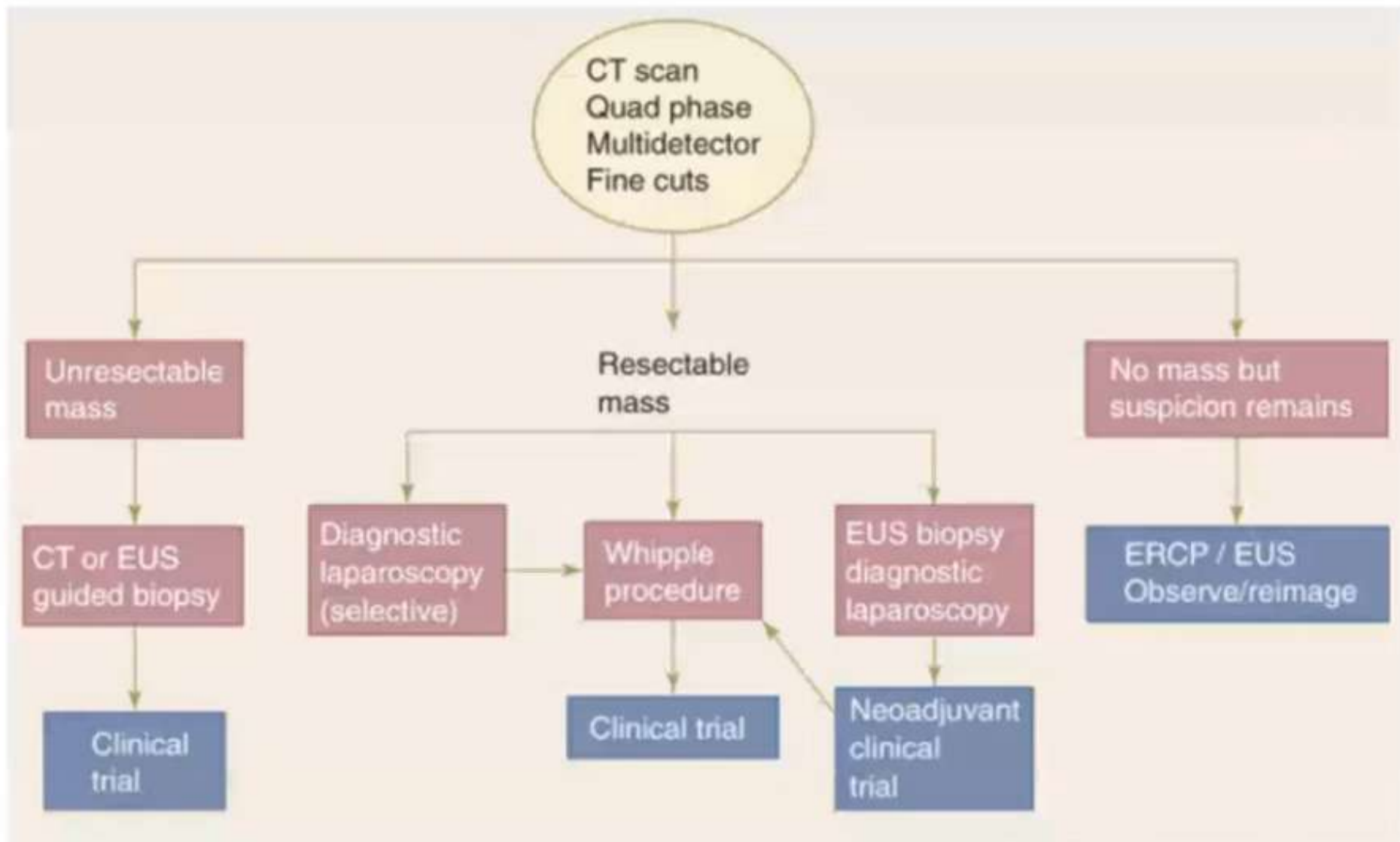


Diagnosis

- **EUS**
 - Detect small pancreatic masses that could be missed by CT scanning.
 - Advantage for transluminal biopsy of pancreatic masses, although a tissue diagnosis before pancreaticoduodenectomy is not required. However, in specific patients a histologic diagnosis may be necessary such as for those in a neoadjuvant clinical trial or before chemotherapy in advanced tumors.
 - EUS is a sensitive test for portal/superior mesenteric vein invasion, although it is somewhat less effective at detecting superior mesenteric artery invasion.
- When all of the current staging modalities are used, their accuracy in predicting resectability is reported to be about **80%**
- **20% laparotomy with no need**

Diagnosis

- **Preliminary laparoscopy** has been advocated for patients with disease felt to be resectable by CT imaging
- Diagnostic laparoscopy with the use of US is reported to improve the accuracy of predicting resectability to about 98%



Palliative Surgery and Endoscopy

- **Pain**

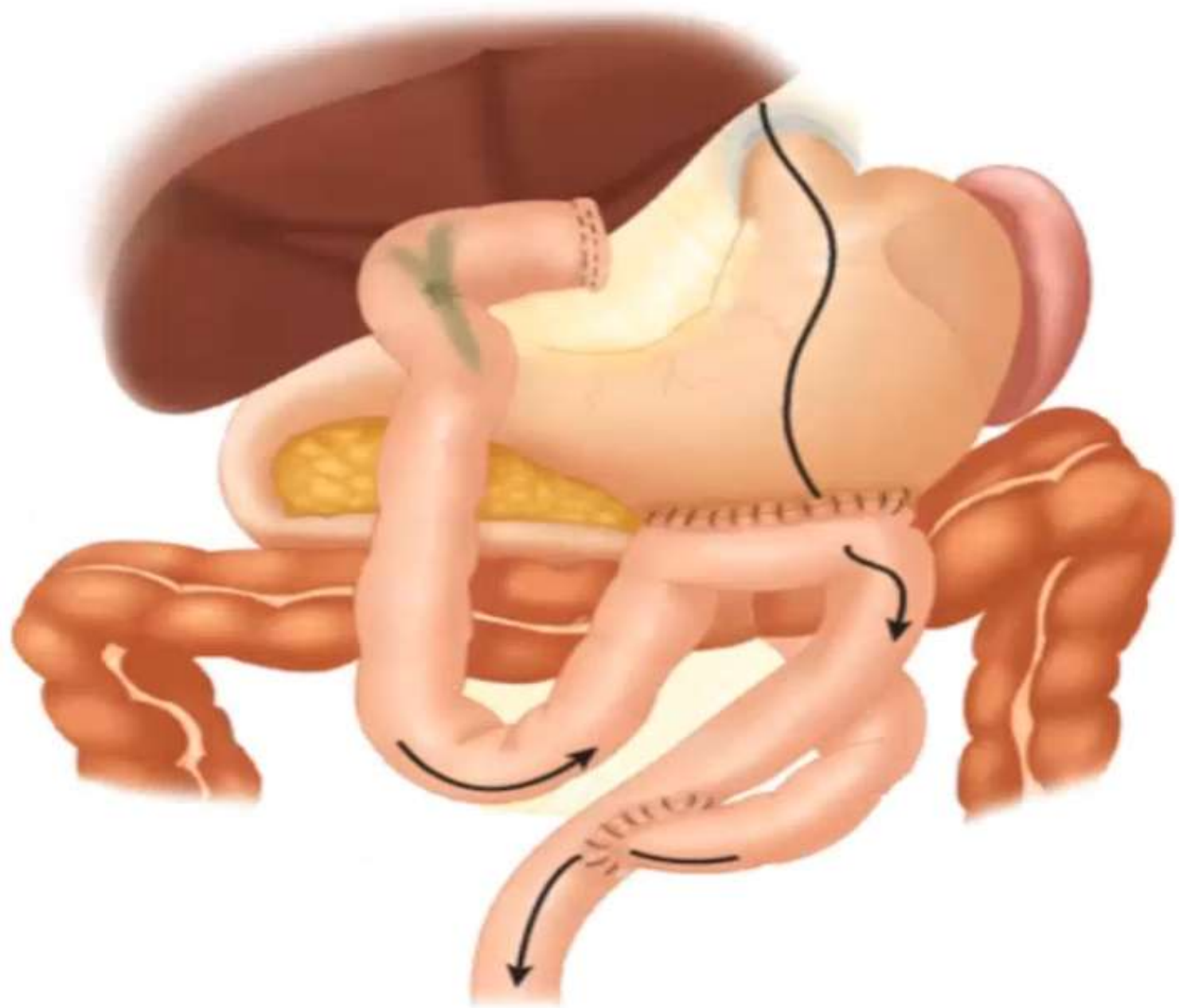
- Oral narcotics: Sustained-release preparations of morphine sulfate
- Celiac plexus nerve block

- **Jaundice**

- Bile duct stent
- Operative bypass: choledochojejunostomy

- **Duodenal obstruction**

- 20% of patients
- Prophylactic?

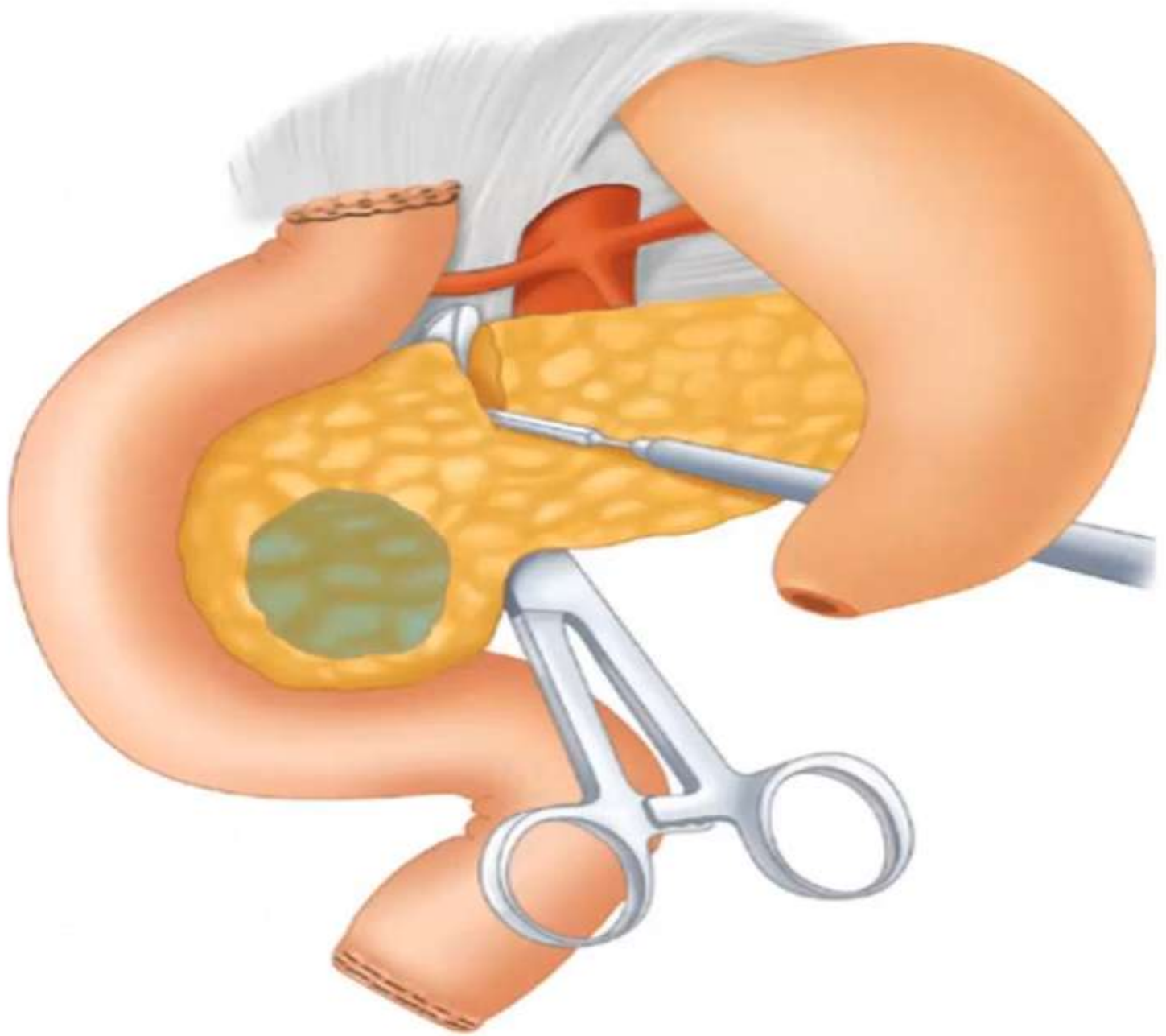


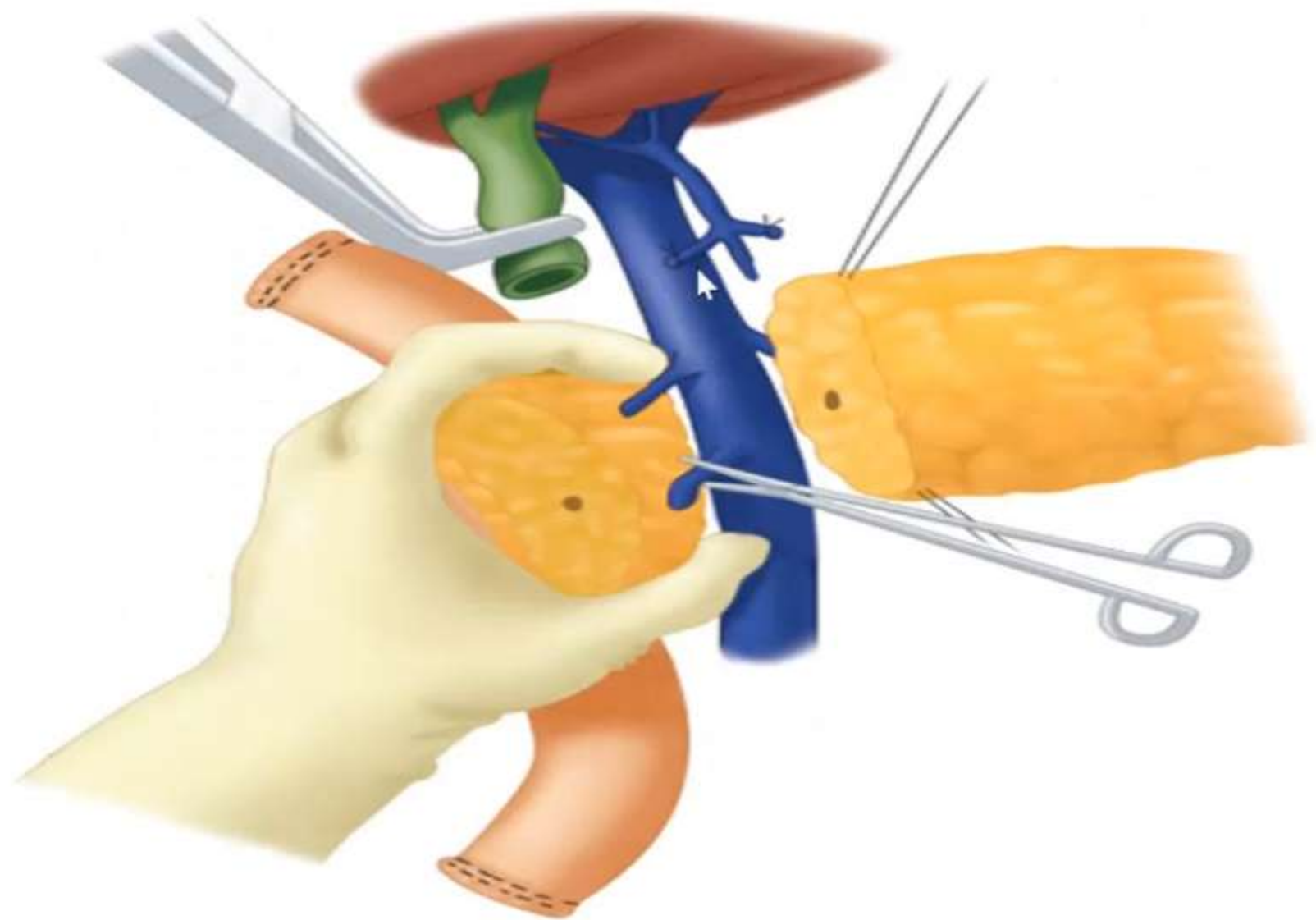
Palliative Chemotherapy and Radiation

- **Gemcitabine**
 - Symptomatic improvement, improved pain control and performance status, and weight gain
 - survival is improved by only 1 to 2 months
- **Erlotinib**
 - very minimal improvement in overall survival in combination with gemcitabine.
- **5-fluorouracil (5-FU) and capecitabine**
 - radiosensitizer in patients receiving radiation therapy

Pancreaticoduodenectomy

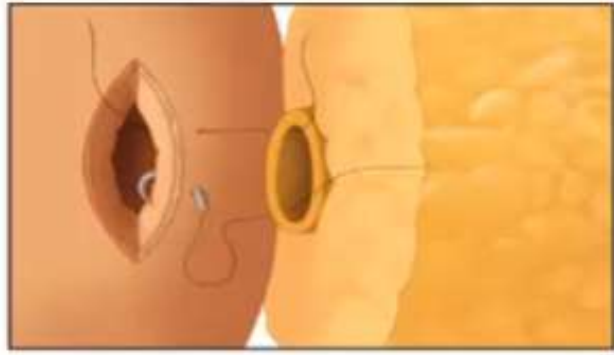
- **Findings contraindicating resection**
 - Liver metastases (any size)
 - Celiac lymph node involvement
 - Peritoneal implants
 - Hepatic hilar lymph node involvement
- **Findings not contraindicating resection**
 - Invasion at duodenum or distal stomach
 - Involved peripancreatic lymph nodes
 - Involved lymph nodes along the porta hepatis that can be swept down with the specimen







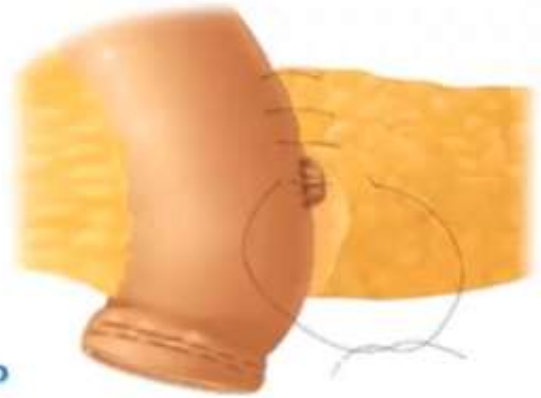
A



B



C



D



E

Complications of Pancreaticoduodenectomy

- The operative mortality rate for pancreaticoduodenectomy <5%
- The most common causes of death are sepsis, hemorrhage, and cardiovascular events
- Postoperative complications are unfortunately still very common, and include delayed gastric emptying, pancreatic fistula, and hemorrhage.