

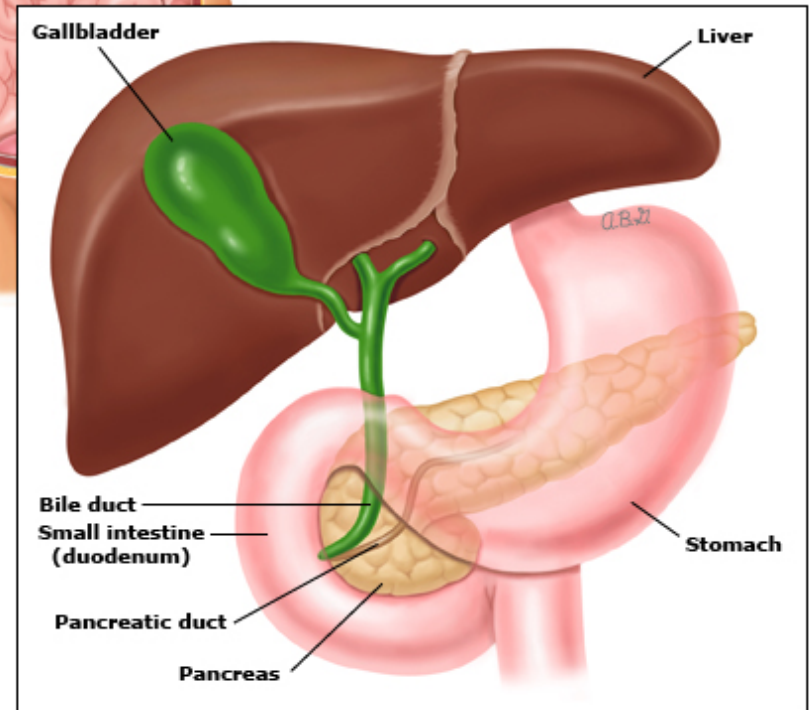
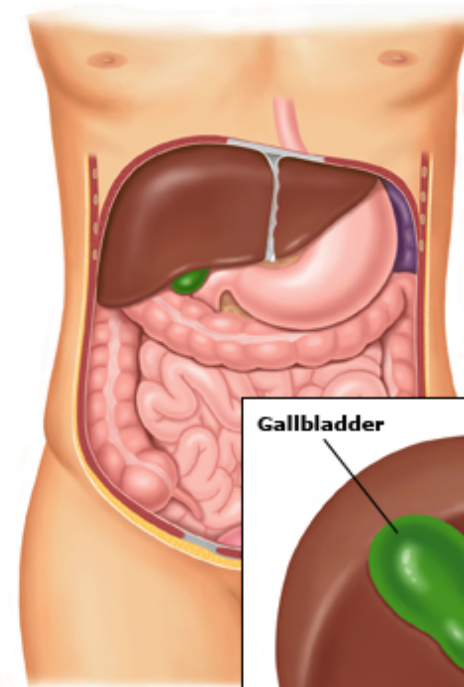
Pancreatic Cancer

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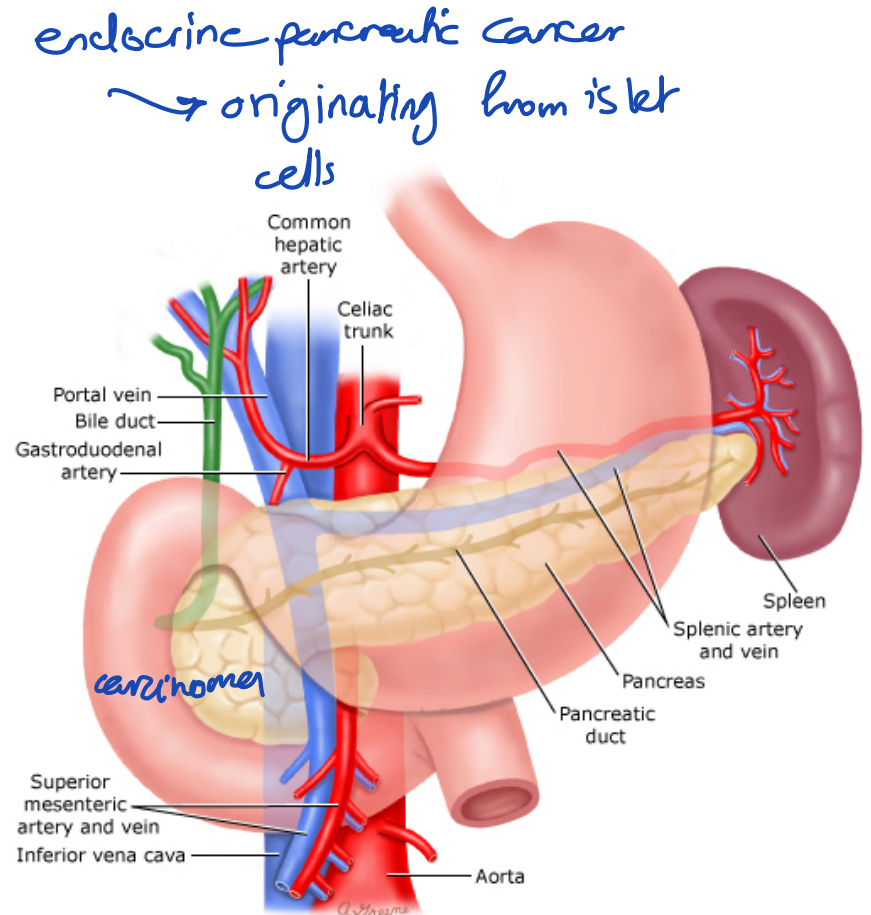
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Introduction

- The pancreas gives rise to several malignant and benign neoplasms
- More than 95% of malignant neoplasms of the pancreas arise from the exocrine elements.
- The commonly used term "pancreatic cancer" usually refers to a ductal adenocarcinoma of the pancreas (including its subtypes), which represents approximately 85 to 90% of all pancreatic neoplasms.
- Neoplasms arising from the endocrine pancreas (pancreatic neuroendocrine [islet cell] tumors) comprise no more than 5%.



→ all the same management and can't detect which subtype is until the whole specimen is out

Epidemiology

- Worldwide, pancreatic cancer is the seventh leading cause of cancer deaths.
- Affects more Western/industrialized parts of the world.
- The disease is rare before the age of 45, Incidence rises sharply thereafter.
- Cases peaked at age 65 to 69 for men and at 75 to 79 for women
- The incidence is greater in males (1.3:1)
- 62% involving the head of the gland, 10% body, 6% tail, and the remainder not determined

Risk Factors

- ① • High fasting plasma glucose
- ② • High body mass index (BMI)
- ③ • Lack of physical activity
- **Environmental risk factors**
- ④ ➤ **tobacco use**, diet, alcohol consumption, and high caloric intake
- ⑤ • Pancreatic cysts
 - ↳ more than 90% are benign but they can develop into malignancy
- ⑥ • Nonhereditary chronic pancreatitis
 - **Hereditary risk factors**
 - Two broad categories:
 - ① defined **genetic predisposition syndromes** and familial pancreatic cancer
 - 5 to 10 percent of individuals with pancreatic cancer have a **family history**

← الدكتور حاذق عن السنين
للخطاطية: المطلوب بين تعرف
! انه في علاقه

Inherited cancer syndromes associated with increased risk of pancreatic cancer

higher risk

Hereditary <u>breast/ovarian</u> cancer	<u>BRCA2, BRCA1</u> <u>PALB2</u>
Familial atypical multiple mole melanoma syndrome	CDKN2A
<u>Peutz-Jeghers syndrome</u>	<u>STK 11</u>
Hereditary nonpolyposis colon cancer (Lynch syndrome)	DNA mismatch repair genes
Hereditary pancreatitis	PRSS1, SPINK1
Ataxia telangiectasia	ATM
Li-Fraumeni syndrome	P53
Familial adenomatous polyposis	APC

Classification

1. Benign — serous cystadenoma.

2. Premalignant lesions

→ most common IPMN (Intraductal Papillary Mucinous Neoplasm)

3. Malignant

• Ductal adenocarcinoma and its subtypes 85-90%.

• IPMN with an associated invasive carcinoma 5%.

• MCN with an associated invasive carcinoma

• Solid pseudopapillary neoplasm

• Acinar cell carcinoma

• Pancreatoblastoma

• Serous cystadenocarcinoma

each one 1% or less

Pathology

The more inclusive term "exocrine pancreatic neoplasms" includes all tumors that are related to the pancreatic ductal and acinar cells and their stem cells (including pancreatoblastoma).

Several subtypes of ductal adenocarcinoma, most have a similar poor long-term prognosis, with the exception of colloid carcinomas, which have a better prognosis, and adenosquamous cancers, which have a worse prognosis.

In general, all are treated similarly.

* If the cancer was in the head or body and presented with jaundice → very poor prognosis and represents liver mets. (always there's mets but here's more than head)

Clinical Presentation

if in the head or uncinete process

→ better than body or tail

The initial presentation of pancreatic cancer varies according to tumor location. Approximately 60 to 70% are localized to the head of the pancreas.

The most common presenting symptoms are pain, jaundice, and weight loss.

usually with the head and uncinete process cancer → earlier presentation → better prognosis

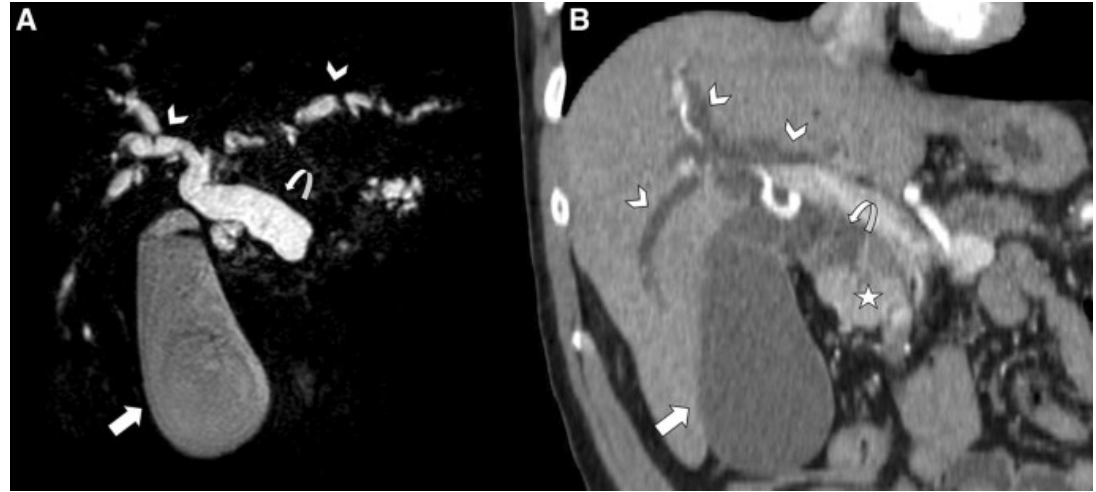
generalized weakness

epigastric pain usually with head and process

✓ Asthenia (most common sign)	✓ Weight loss
✓ Anorexia	✓ Abdominal pain
✓ Dark urine	✓ Jaundice
✓ Nausea	✓ Back pain → body and tail
✓ Diarrheal	✓ Vomiting
✓ Steatorrhea	✓ Thrombophlebitis hypercoagulable state

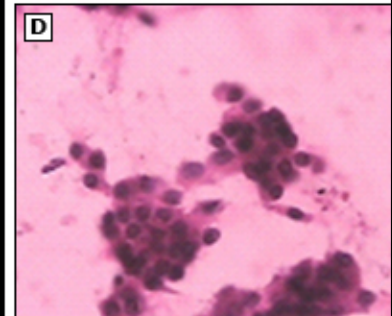
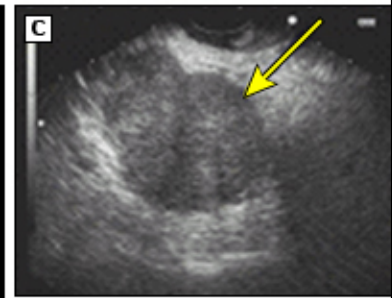
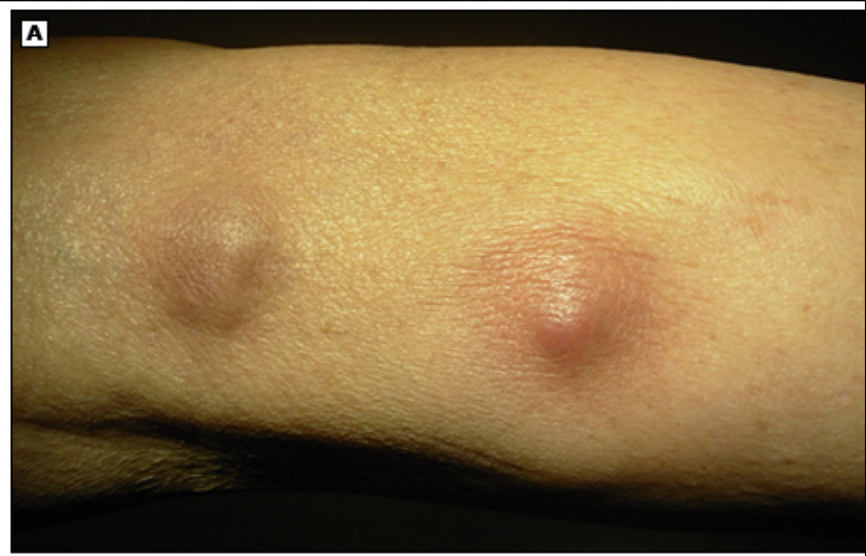
The most frequent signs:

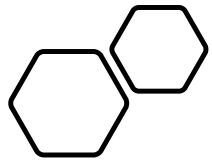
- * ● Jaundice 60%
- * ● Hepatomegaly 30%
- * ● Right upper quadrant mass 12%
- * ● Cachexia
- * ● Courvoisier's sign (nontender but palpable distended gallbladder at the right costal margin) 10-15%
- * ● Epigastric mass
- * ● Ascites



- Unexplained superficial thrombophlebitis, which may be migratory (classic Trousseau's syndrome), is sometimes present and reflects the hypercoagulable state that frequently accompanies pancreatic cancer.
- Rarely, erythematous subcutaneous areas of nodular fat necrosis, typically located on the legs (pancreatic panniculitis).

— nondiagnostic, present in other conditions





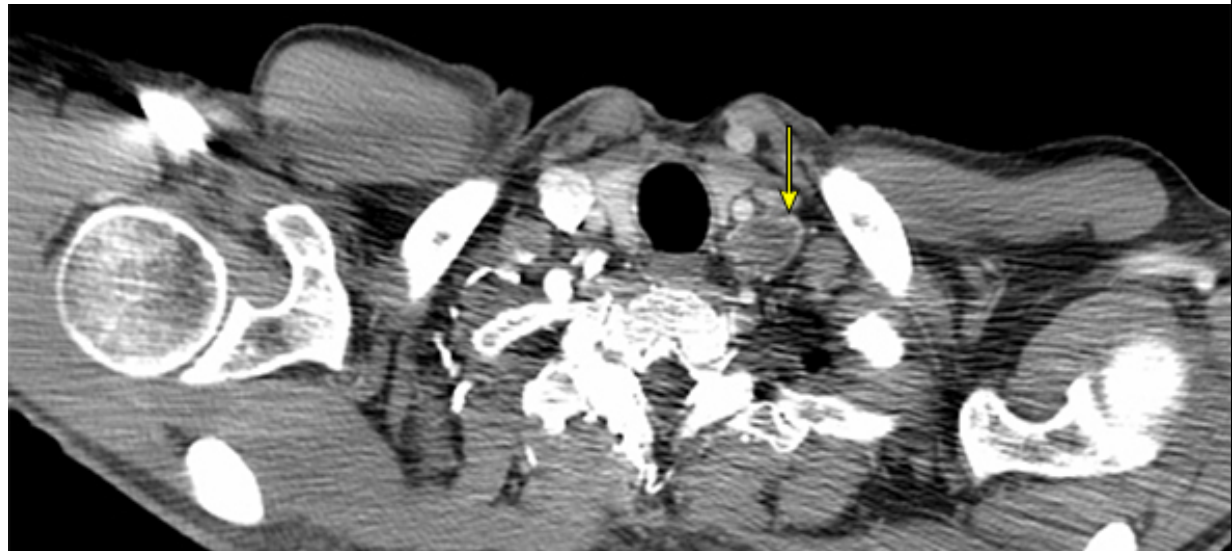
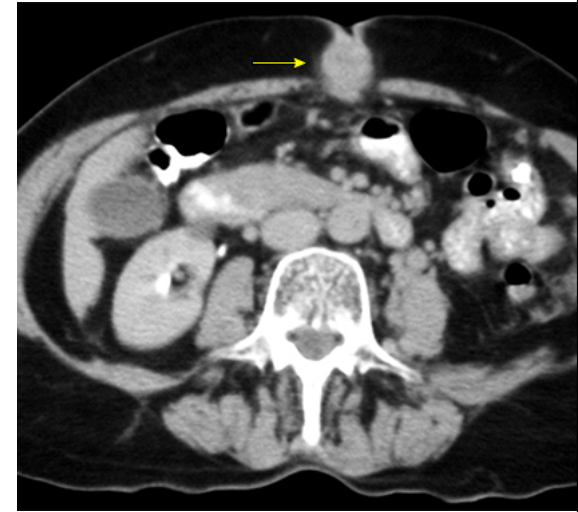
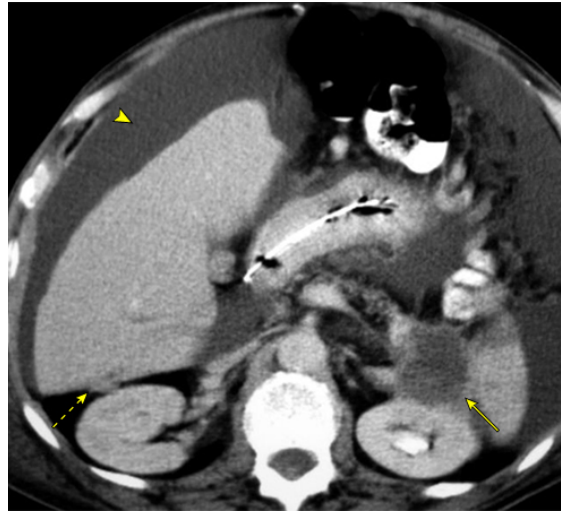
80% patient → no Surgery
20% surgery / 1/4 → irresectable intra-op.

Metastatic disease most commonly affects the liver, peritoneum, lungs, and less frequently, bone.

Signs of advanced, incurable disease:

- * ● An abdominal mass.
- * ● Liver metastases.
- * ● Ascites.
- * ● Left supraclavicular lymphadenopathy (Virchow's node).
- * ● A palpable periumbilical mass (Sister Mary Joseph's node)

↳ 10-15% , other cancers: gastric ovarian



* Margins after tumor resection =

R_0 : free margins (completely excised)

R_1 : microinvolvement (microscopic)

R_2 : macroinvolvement
قصبت و هزل باقي
طاقورن اقبير
كلل

Differential Diagnosis

not very suggestive ↗
also

→ Most early sign between these 3
painless jaundice

→ even with this 5-year survival: 30-40%

The signs and symptoms associated with pancreatic cancer are often nonspecific, so the differential diagnosis is large. *wide differential diagnosis*

Three of the more common findings leading to suspicion for pancreatic cancer are jaundice, epigastric pain, and weight loss.

The positive predictive value of these symptoms for the diagnosis of pancreatic cancer is low, with the possible exception of jaundice in an older patient.

Conjugated Hyperbilirubinemia

Intrahepatic cholestasis	Extrahepatic cholestasis (biliary obstruction)
Viral hepatitis/ Chronic hepatitis/ End-stage liver disease	Choledocholithiasis
Alcohol-associated hepatitis/ Non-alcohol-associated steatohepatitis	Intrinsic and extrinsic tumors (eg, cholangiocarcinoma, pancreatic cancer)
Primary biliary cholangitis/ Following organ transplantation	Primary sclerosing cholangitis
Drugs and toxins (eg, alkylated steroids, chlorpromazine, herbal medications [eg, Jamaican bush tea], arsenic)	AIDS cholangiopathy
Sepsis and hypoperfusion states/ Total parenteral nutrition	Acute and chronic pancreatitis
Infiltrative diseases (eg, amyloidosis, lymphoma, sarcoidosis)	Strictures after invasive procedures
Pregnancy	Certain parasitic infections (eg, <i>Ascaris lumbricoides</i> , liver flukes)
Postoperative cholestasis	Defect of sinusoidal reuptake of conjugated bilirubin.. Rotor syndrome
Hepatic crisis in sickle cell disease	Defect of canalicular organic anion transport Dublin- Johnson syndrome

*IF CA19.9 is very high → consider mets.

Very common scenario ←

Presentations male - late 60s - diagnosed with DM lately - weight loss intentionally vague abdominal pain - anorexia - asthenia - dark urine

Diagnostic Approach

* Sometimes the patient come with acute abdominal pain similar to acute pancreatitis so we should measure lipase and amylase.

❖ Initial testing

- Routine laboratory tests are often abnormal but are not specific for pancreatic cancer. Common abnormalities include an elevated serum bilirubin and alkaline phosphatase levels, and the presence of mild anemia.
- Abdominal imaging (Transabdominal ultrasound/ Abdominal CT)

❖ Subsequent testing if initial imaging is positive

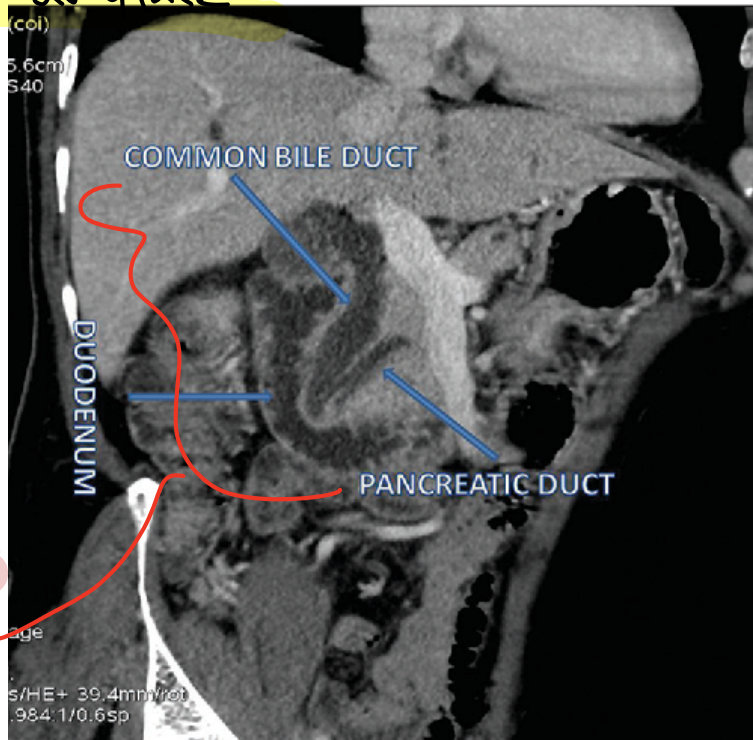
- a CT with "pancreatic protocol"
- Tumor markers (CA19.9)

non specific if jaundice →

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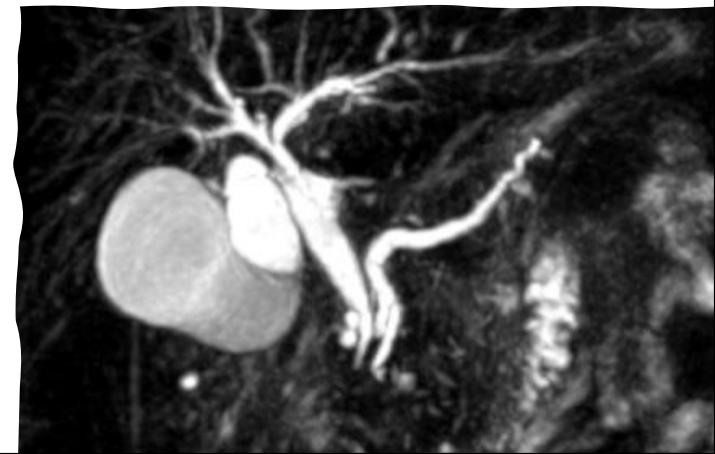
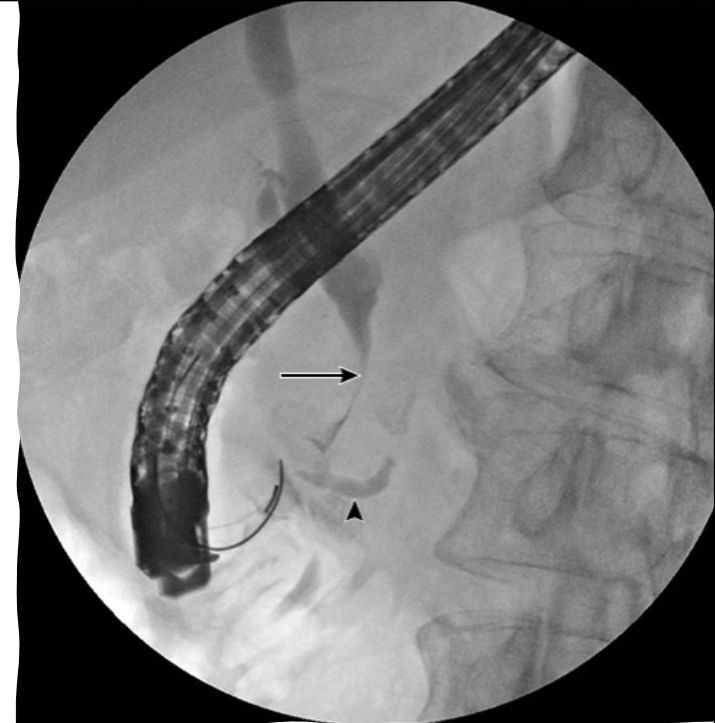
Go to surgery immediately without biopsy ←

double duct sign ←



* CA19.9 if (-) → doesn't rule out

-
- **Endoscopic retrograde cholangiopancreatography**
 - ERCP provides an opportunity to collect tissue samples (forceps biopsy, brush cytology) for histologic diagnosis → accuracy 20-30%.
 - **Magnetic resonance cholangiopancreatography (more)**
 - Dilatation of both the pancreatic duct and the common bile duct, commonly referred to as the "double duct sign"



used also in rectal tumor

Endoscopic Ultrasound

→ ultrasound on the top of the endoscope

↳ biopsies either core or cells and more sensitive than ERC

- An endoscopic ultrasound (EUS)-guided biopsy may be recommended if a diagnosis of chronic or autoimmune pancreatitis is suspected
- ✓ Based on history (eg, extreme young age, history of alcohol use disorder, history of other autoimmune diseases)
- ✓ Or based on other imaging (eg, multifocal biliary strictures (suggestive of autoimmune pancreatitis) or diffuse pancreatic ductal changes (suggestive of chronic pancreatitis)).
- Endoscopic ultrasound (EUS)-guided or percutaneous biopsies, though this is not always required in patients who appear to have potentially resectable disease and who have typical imaging findings.

عسری
History
سوزش
Pancreatic
CA

*Also used in local invaded patients



*Don't insist on biopsy → double duct sign → pancreatic CA until proven otherwise unless a very strong evidence (5-year old child for example)

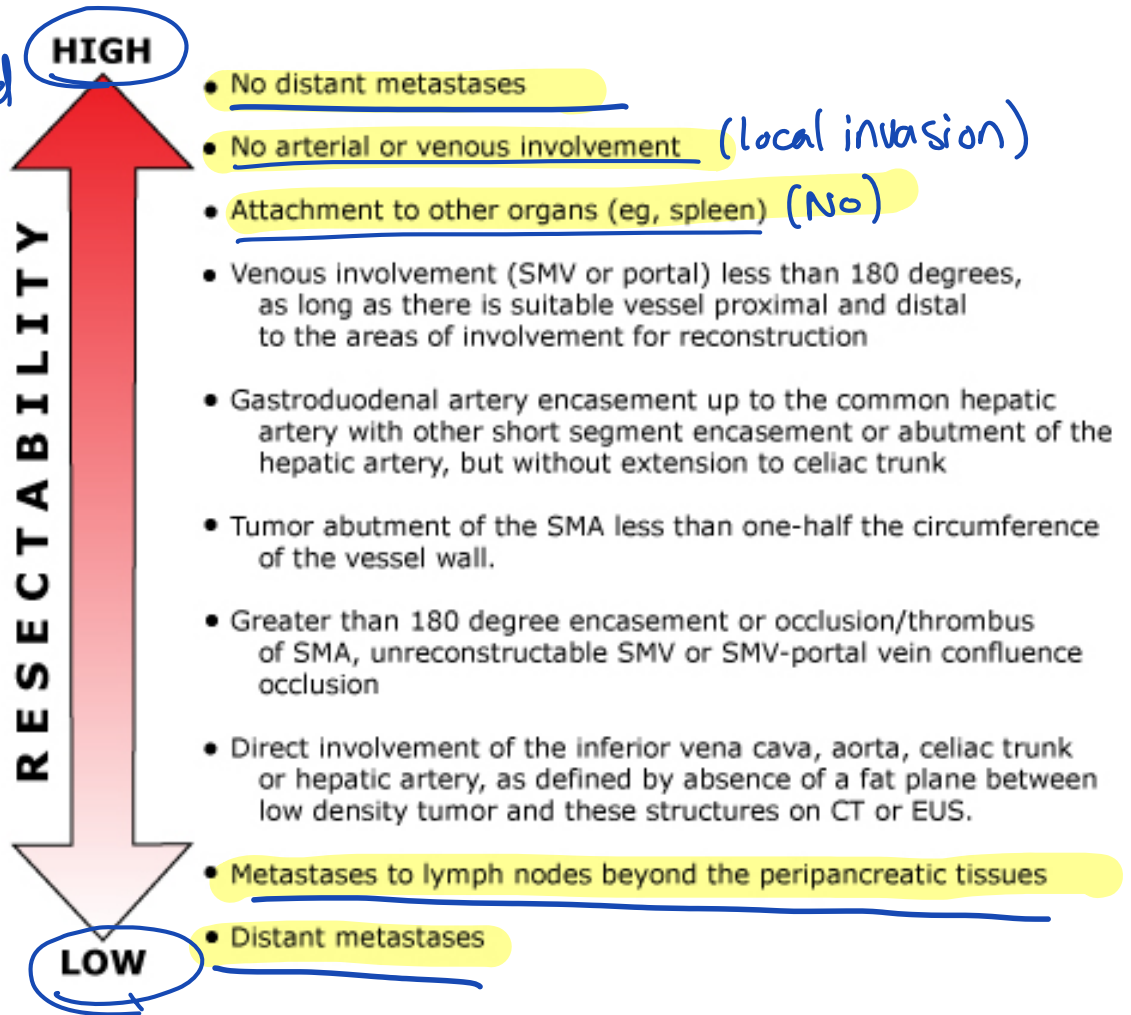
Assessing Resectability

→ PET CT scan

- Complete surgical resection is the only potentially curative modality of treatment for pancreatic cancer.
- In general, pancreatic cancers are categorized on a continuum from resectable to unresectable according to the involvement of adjacent structures and the presence of distant metastases
- Unfortunately, only 15 to 20 percent of patients are candidates for pancreatectomy

*We don't use PET CT Scan that much in pancreatic CA, not specific
IF the patient is DM with uncontrolled blood glucose, inflammation ----

Continuum of resectability for pancreatic adenocarcinoma

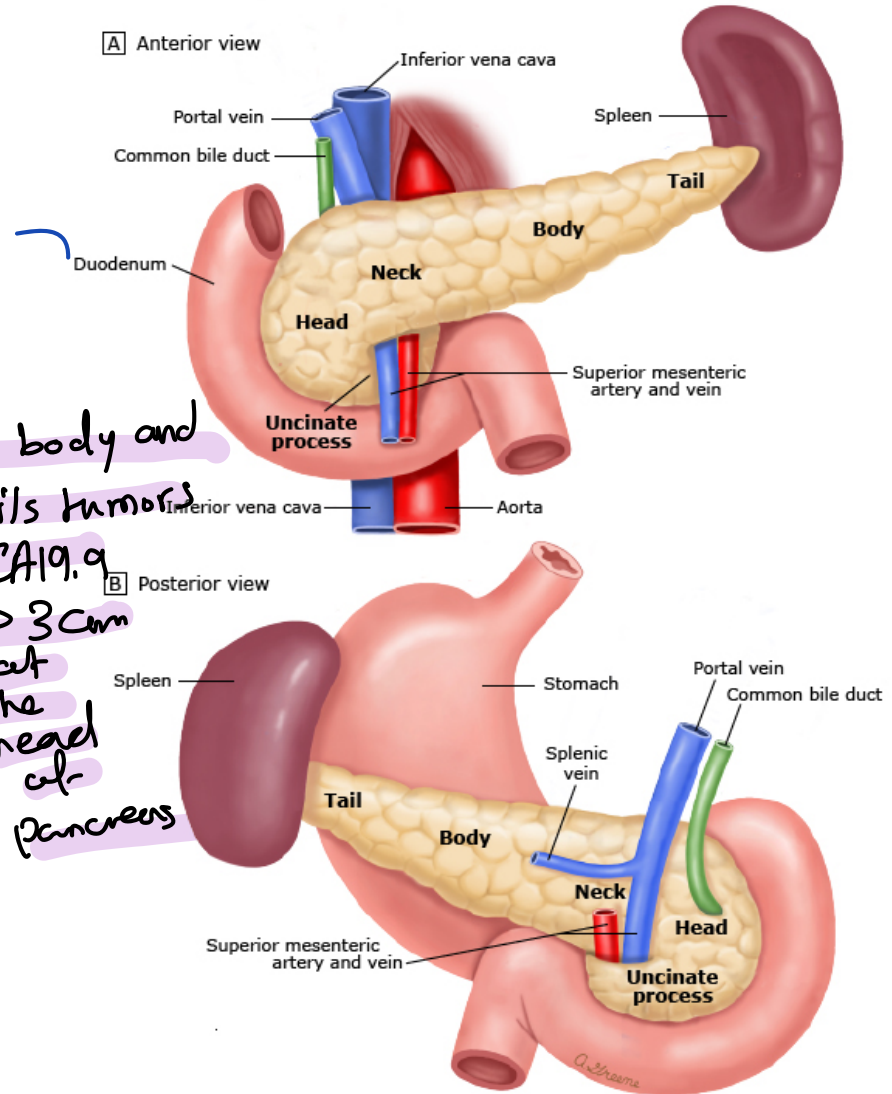


Preoperative Considerations

- Staging Laparoscopy → if there's mets used in large body and tails tumors
- Role Of Preoperative Biliary Drainage
- Role Of Neoadjuvant Chemotherapy

→ jaundice patient if bilirubin ≤ 15 (we don't prefer stents because foreign body)

→ border line resectable



tails tumors
 - \uparrow CA19.9
 - > 3 cm at the head of pancreas

Surgical Management

- **Tumors in the head of the pancreas**

Pancreaticoduodenectomy (Whipple procedure)

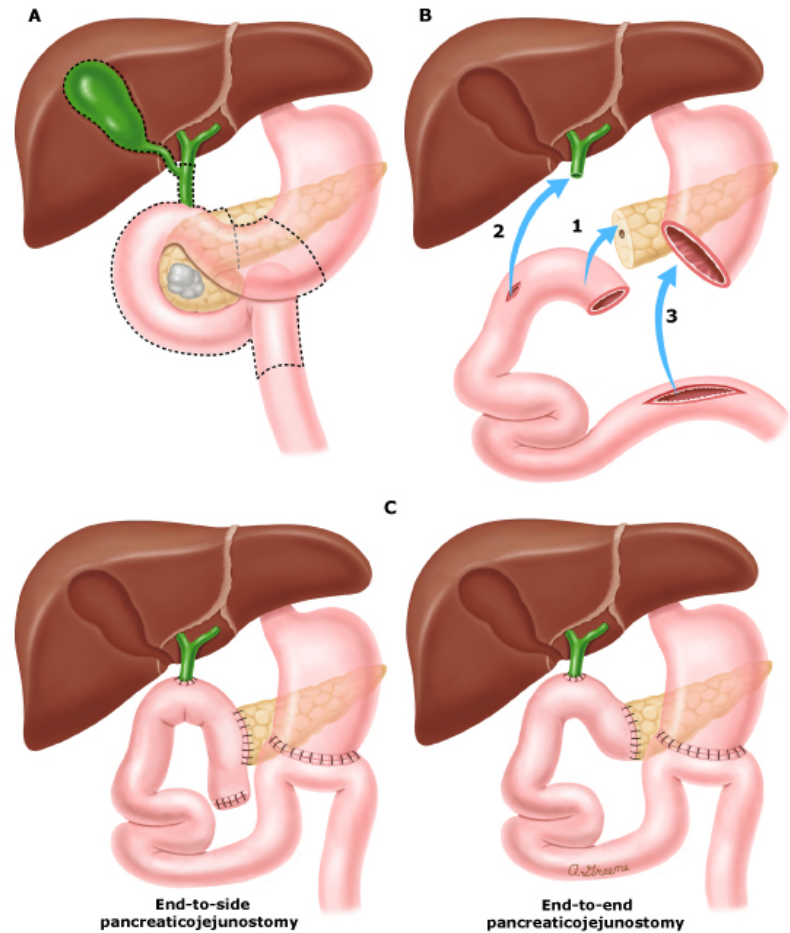
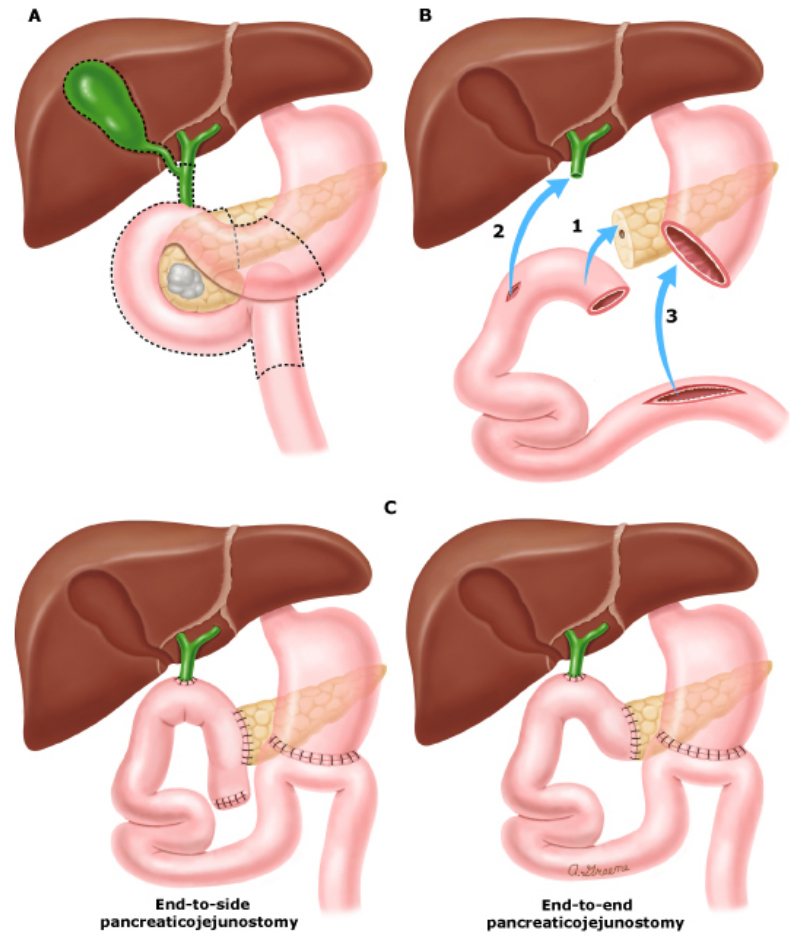
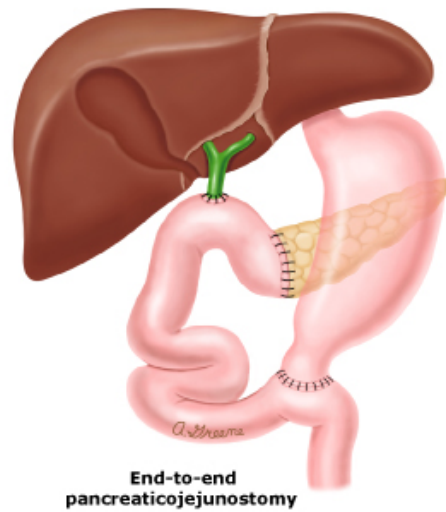
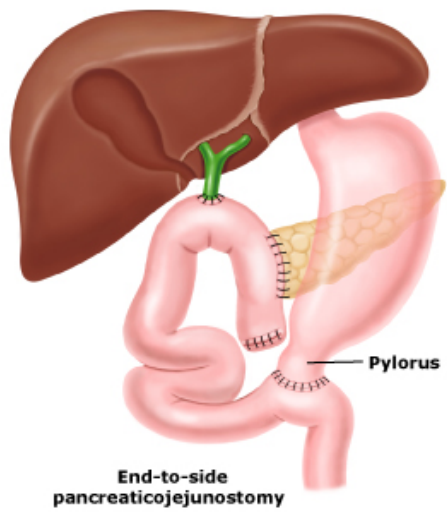
- **Tumors in the body or tail**

Distal subtotal pancreatectomy, usually combined with splenectomy.

- **Tumors involving the entire gland** (worst scenario)

Total pancreatectomy, however, the metabolic consequences of total pancreatectomy, include permanent exocrine insufficiency and brittle diabetes

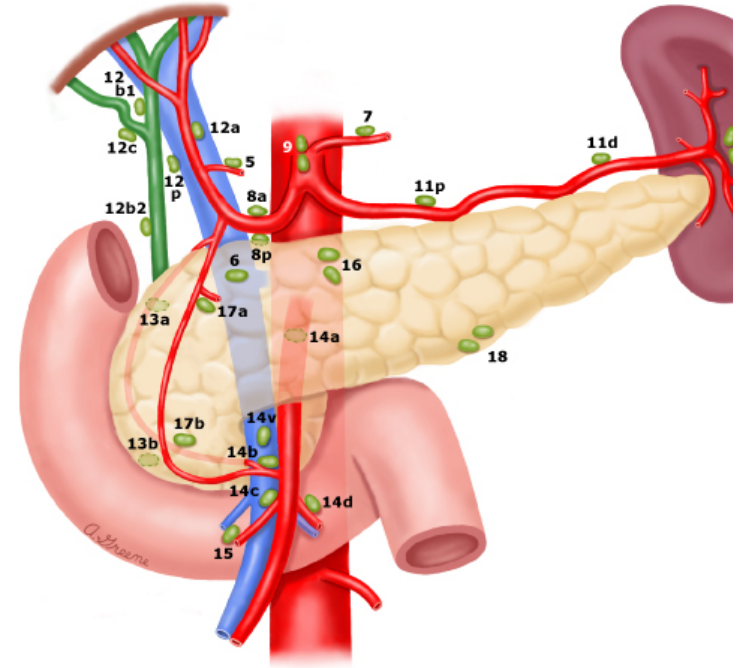
main
complication



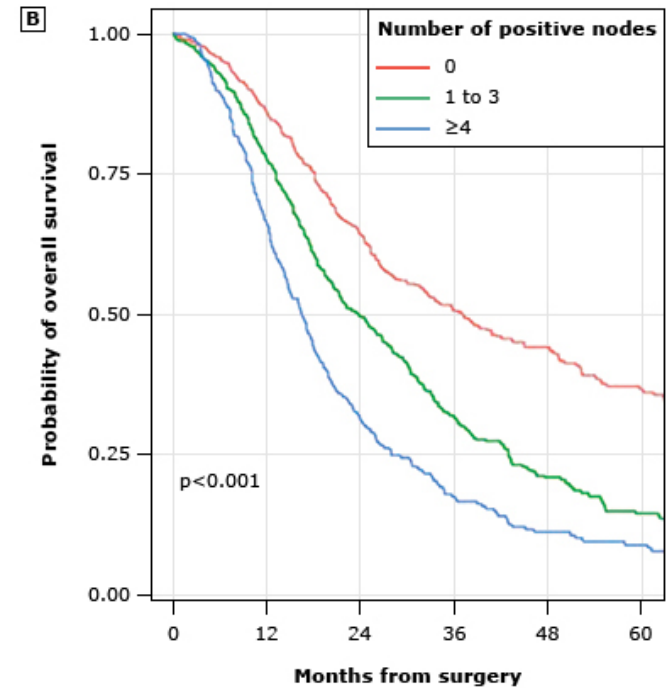
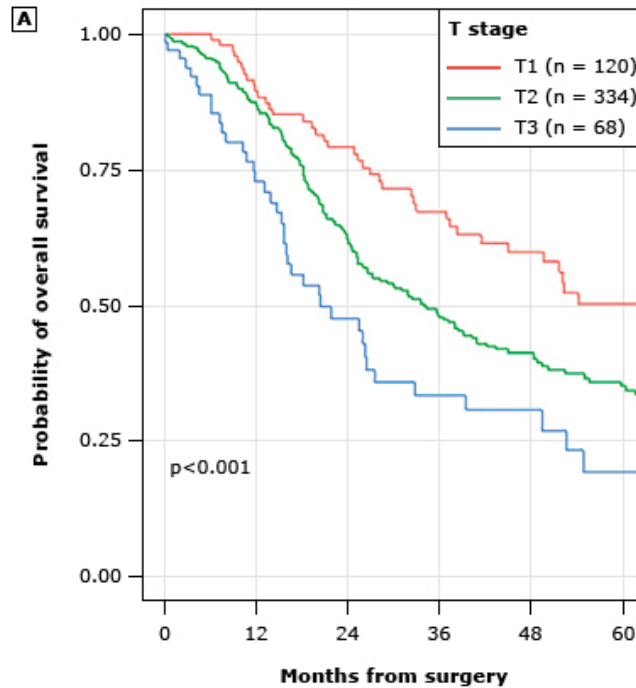
Tx → further assessment

Prognosis and Prognostic Factors

- The most important prognostic factor for completely resected patients is nodal status.
- Tumor stage is the most important prognostic factor (TNM) classification
- The status of the surgical margins (involved or uninvolved)
- Tumor differentiation
- The presence or absence of lymphatic invasion
- Both preoperative and postoperative serum CA 19-9 levels,
- Cigarette smoking



Outcomes of pancreaticoduodenectomy



- Cancer of the exocrine pancreas is a highly lethal malignancy.
- Surgical resection is the only potentially curative treatment.
- Unfortunately, only 15 to 20% of patients are candidates for pancreatectomy.
- Furthermore, prognosis is poor, even after a complete resection.
- The five-year overall survival for stage ia pancreatic cancer nearly doubled from 45% to 84%.
- These trends were attributed to improved early diagnosis and detection.

