Malignant tumours of the liver &pancreas

Dr .Tayseer Al-tawarah

Hepatobiliary &pancreatic surgeon

Assistant professor /Hashemite University

Liver tumour

Primary

- HCC
- Intra hepatic cholangiocarcinoma
- cystadenocarcinoma
- Other (EHE, Lymphoma, angiosarcoma)

Secondary

(most common)

- CRLM
- NET
- Others (gastric , oesophagus , breast , melanoma , GIST , RCC , ovarian , testicular)

Primary
1- HCC(Hepatocellular carcinoma)

- The most common primary hepatic tumour
- The fourth Cancer related death worldwide
- Arising on background of the underlying liver cirrhosis in 80-90%
- 10-20% no underlying Cirrhosis but not a normal liver
- Hight risk for vascular invasion , multifocality and advance at presentation

- The geographic distribution of HCC varies widely according to ethnic groups and regions, with a clear association with exposure to hepatitis viruses and environmental pathogens- more in sub-Sahara Africa and south Asia
- The risk of tumour development varies with the type of cirrhosis; the highest risk is reported for chronic viral hepatitis, whereas lower risks are associated with other forms of cirrhosis such as primary biliary cirrhosis.

- HCC in the absence of cirrhosis may be related to some of the same aetiologies as those responsible for HCC in cirrhotic livers such as HBV infection or alcohol abuse.
- Alternatively, HCC may occur as a result of conditions that infrequently lead to cirrhosis such as α1-antitrypsin deficiency, haemochromatosis, or in the setting of specific aetiologies that do not result in cirrhosis such as hormonal exposure or glycogenosis
- Male >female

Risk factor

- Chronic HBV infection: the most frequent risk
- HCV infection
- Alcohol
- Non-alcoholic fatty liver disease (NAFLD)
- Obesity and diabetes also increase the risk of HCC
- Hereditary haemochromatosis
- Cirrhosis of other aetiologies(PBC, auto-immune hepatitis)
- Aflatoxin
- Metabolic liver diseases and HCC(α1- antitrypsin deficiency, porphyria cutanea tarda, tyrosinaemia and hypercitrullinaemia.)
- Adenoma, contraceptives and androgens

Clinical presentation

- Abdominal pain (MC)
- Weight loss
- Rupture 5-15%
- Symptoms and signs of advance liver disease
- Hepatomegaly
- Constitutional symptoms

Diagnosis

Either on screening program for high-risk Cirrhotic patient or in patient evaluated for deranged LFTs or cancer related symptoms

Bloods –LFTs usually reflect the underlying liver disease , jaundice usually related to decompensated liver rather than tumour compression

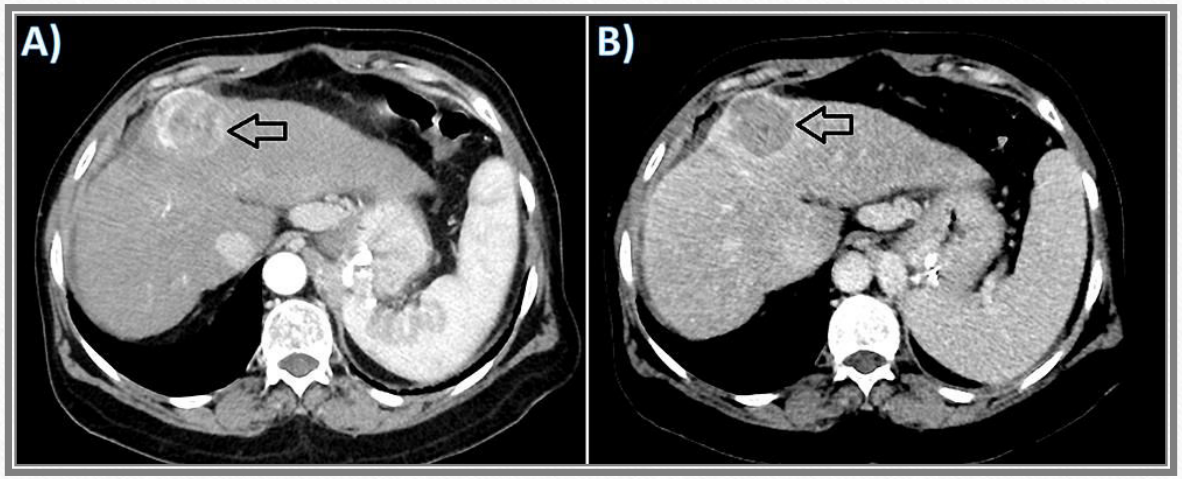
US, Triple phase liver CT , Liver MRI

tumour marker : A-FB (normal 0-20) High in 70-80%

Level >400 consider diagnostic

>10000 Associated with poor differentiation and vascular invasion

- CT feature of typical HCC
- **Typical feature of early arterial contrast enhancement and early washout out in the delayed phase on both CT and MRI**
- Always remember that the liver tumors either primary and secondary received their blood supple predominately from the hepatic artery not the Portal vein



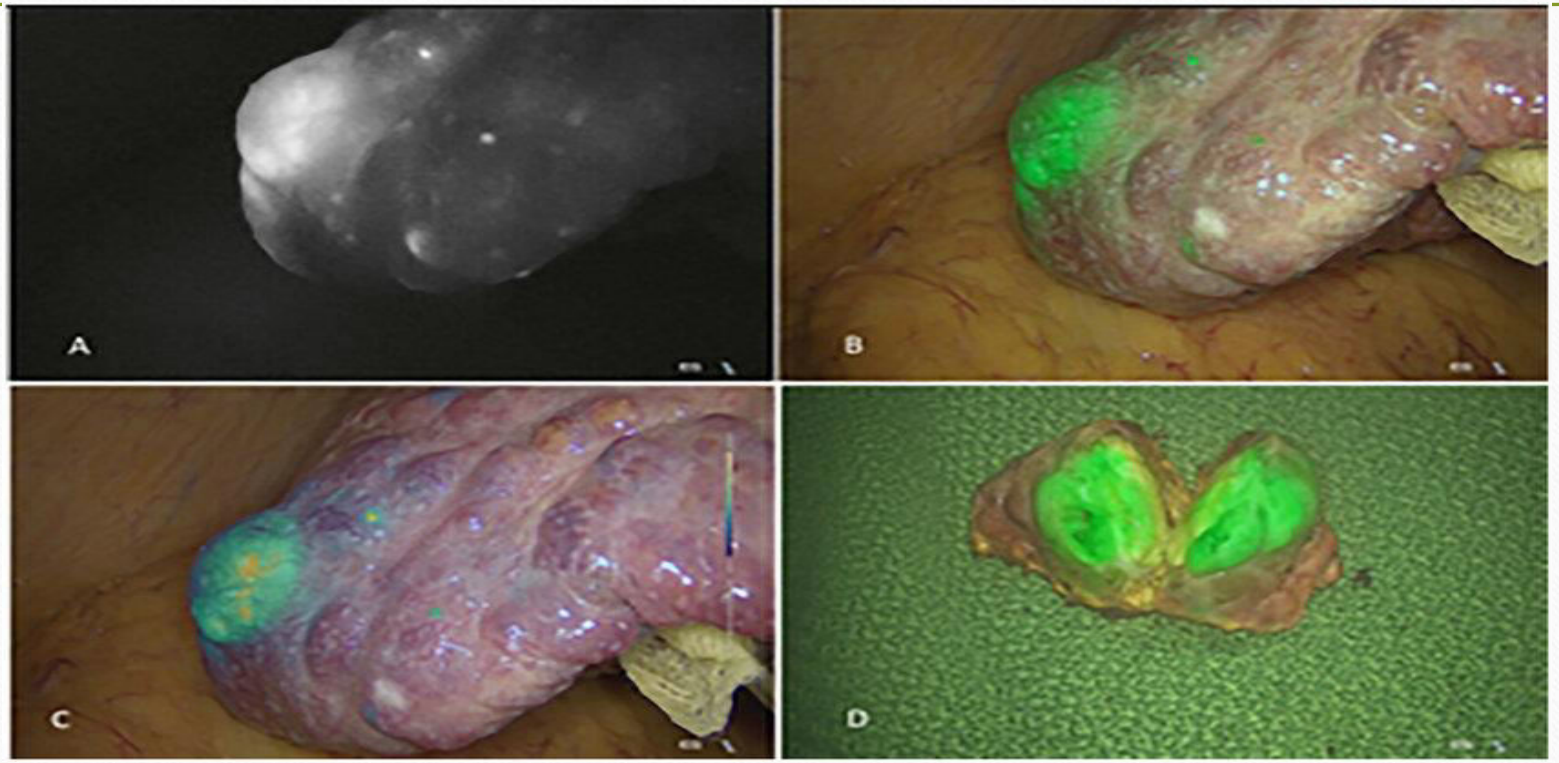
- Remember: Only 15-20% of HCC is resectable, because rest of the tumors have • Multicentricity, Bilobar involvement Portal vein invasion, Lymphatic metastasis
- pre operative biopsy isn't mandatory for diagnosis in typical images feature
- Evaluation of the underlying liver disease and the stages of liver Cirrohis is mandatory using CPS or MELD score

Treatment

- MDT decision not single surgeon decision
- CPS stage of Cirrhosis , performance status of the patient , number and the size of the tumour , extrahepatic metastasis and FLR ,all should be consider before making the decision of the treatment
- A lot of the staging system are used to stage the tumour (GRETCH ,CLIP CUPI, and TNM)
- BCLC guild line for management are most widely used

Cont . Treatment

- Curative : hepatectomy , liver transplant , RFA in absence of decompensated liver
- TACE and systemic therapy (Sorafenib) are the two palliative treatment modality that improve the survival in patient not candidate for curative treatment in absence of decompensated liver
- Best suppurative care and symptoms palliation in advance decompensated liver or not fit for any other treatment option (child C stage)
- No role for neo-adjuvant or adjuvant chemotherapy


A
B
C
D

- Tumour recurrence is the major cause of death following resection of HCC in the cirrhotic patient. Its incidence is 40% within the first year
- 5- and survival rates of 43.9%
- Independent predictors of survival were age, degree of liver damage, AFP level, tumour diameter, number of nodules, vascular invasion and surgical margins.
- Best survival in case of small <2cm encapsulated tumour in patient with child A score

Fibrolamellar HCC

- Occurs in young adults without underlying cirrhosis
- Non-encapsulated but well, circumscribed, so high resectability rate
- Grows slowly and has better prognosis
- F>M
- AFP elevated in less than 10%
- Long-term survival can be expected in about 50-75% of patients after complete resection
- Recurrence is common and occurs in at least 80% of patients
- Presence of lymph node metastases predicts a worse outcome

Intrahepatic cholangiocarcinoma (ICCA)

- Is the second most frequent primary tumour of the liver after HCC.
- It arises from the peripheral intrahepatic biliary radicles
- In the Western world, the incidence of ICCA is 0.3–3 per 100000
- biliary intraepithelial neoplasia. and the intraductal papillary neoplasm of the bile duct are the two lesion usually precede invasive cholangiocarcinoma
- This tumour carries poor prognosis as it diagnosed at advance stage
- Equally between male and female , between the age of 55 and 75 years.

Risk factors

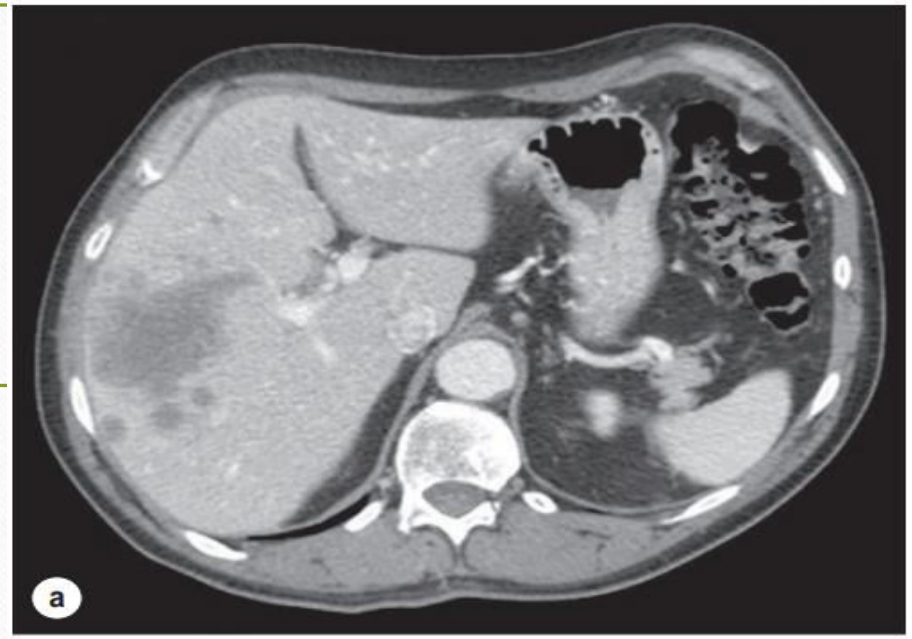
- in most patients with ICCA (more than 95%) none of these risk factors can be identified
- chronic biliary inflammation such as primary sclerosing cholangitis, chronic choledocholithiasis, hepatolithiasis, parasitic biliary infestation, Caroli's disease and choledochal cyst.
- New risk factors are emerging, including chronic non-alcoholic liver disease, HBV infection, HCV infection, diabetes and the metabolic syndrome.
- However, in contrast to HCC, most ICCAs develop without a background of liver disease.
- In surgical series, 75% of patients have normal livers, 16% have chronic hepatitis/liver fibrosis and 9% have cirrhosis

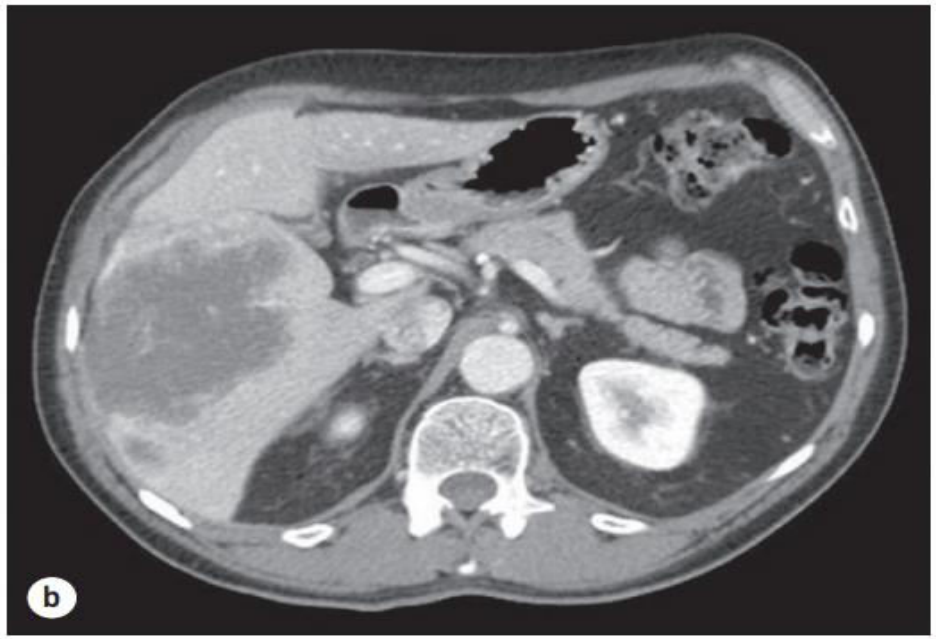
Clinical presentation and lab tests

- abdominal pain, malaise, night sweats, asthenia, nausea and weight loss.
- jaundice may be present if the tumour compresses or invades the biliary confluence.
- LFTs non-specific even though an increase in liver enzymes (in particular GGT) may be the only initial finding in some patients
- Serum markers (Ca19.9, CEA) lack sensitivity and specificity.

Imaging

- Liver CT and liver MRI are used in diagnosis
- They are typically large, non-encapsulated, heterogeneous, associated with narrowing of adjacent portal veins and retraction of the liver capsule
- satellite nodules frequently develop in the vicinity of the tumour, and subsequently in the contralateral lob
- high propensity for lymph node invasion





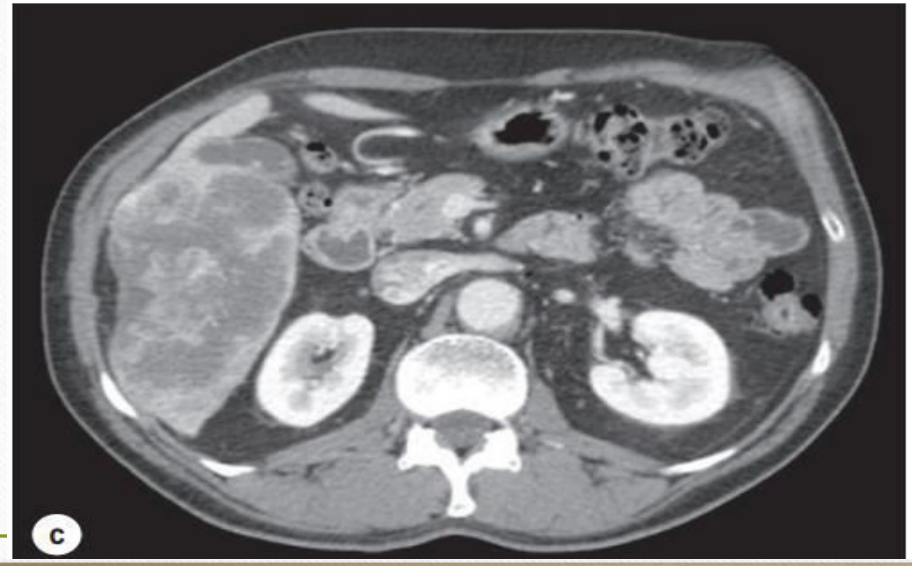


Figure 5.7 • CT of a patient with an intrahepatic/peripheral cholangiocarcinoma. Note the presence of typical satellite nodules at the periphery of the tumour **(a)**, the absence of vascular uptake **(b)** and the retraction of the capsula **(c)**.

Types

- Mass forming (MC)
- Intraductal-growth- rare but have a better long-term prognosis.
- Infiltrating type : ICCAs have a worse prognosis than the mass forming type due to spread along Glisson's capsule and high incidence of lymph node involvement
- Mixed type

Treatment

Surgical resection is the only curative treatment.

Unlike HCC, there is currently no place for liver transplantation except in very selective case

There is a significant risk (20–30%) that, despite adequate preoperative imaging, contraindications to a curative resection are identified at laparotomy

Staging laparoscopy has been advocated

Systemic therapy in un resctable tumours

Biliary Cystadenocarcinoma

- Rare malignancy, typically intrahepatic in location. May arise from preexisting biliary cystadenomas.
- Female to male ratio is 2 : 1
- CA 19-9 is raised
- The presence of an associated ovarian-like stroma in female patients appears to signify a favourable prognosis
- Tends to be multilocular, fluid from the cyst can be blood stained, clear, or bile tinged.
- Preoperative cyst aspiration is not recommended because there is a risk for peritoneal tumour seeding

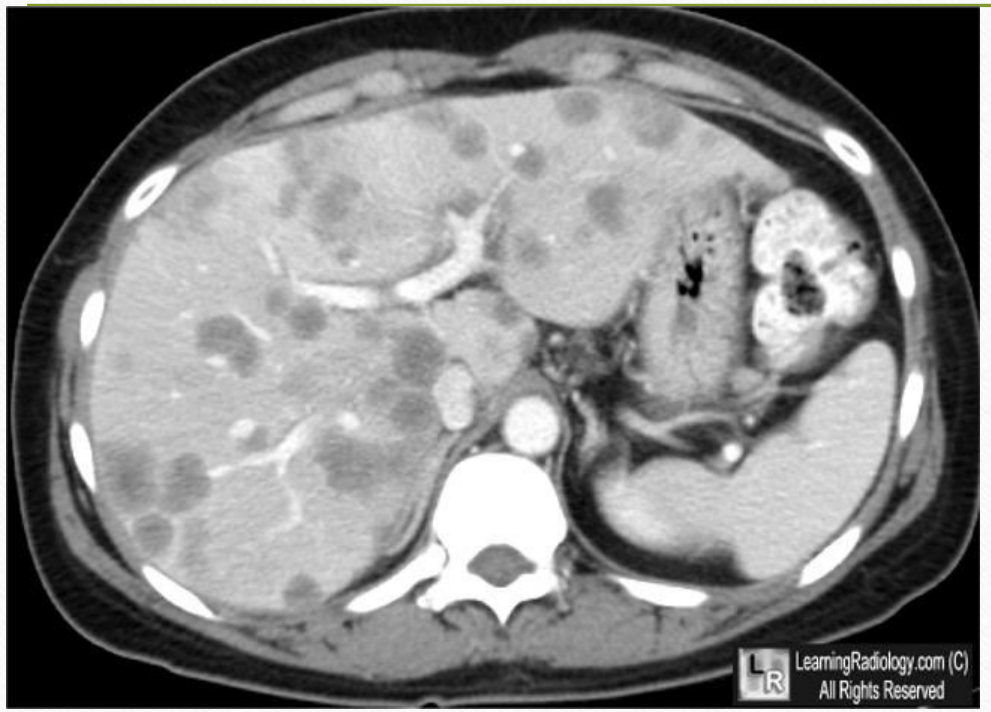
- The only potentially curative treatment is complete removal, by a major liver resection with clear margins.
- Survival rates for this disease have been reported in the range of 25% to 100% at 5 years

Colo-rectal liver metastasis

- The liver is the most frequent site of metastases from CRC, with liver disease being detected either at the time of CRC diagnosis (synchronous; 20–25%) or subsequently (metachronous; 40%).
- The extent of liver disease is a key determinant of survival in patients with isolated colorectal liver metastases (CRLM).
- The diagnosis of CRLM is usually based on imaging during evaluation of patients with CRC , Rarely FNA biopsy

Imaging

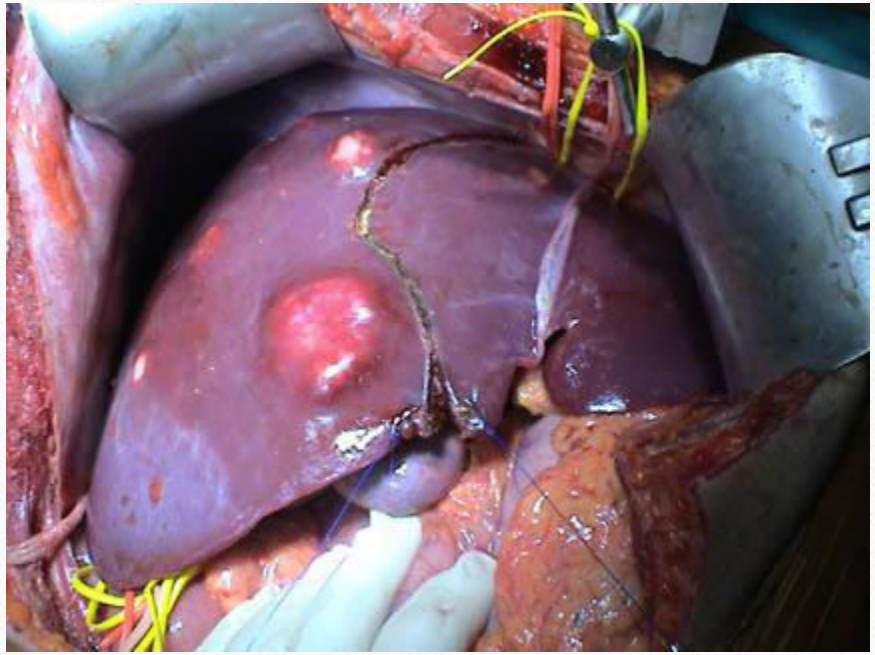
- US is not a sensitive diagnostic test for CRLM and can fail to identify over 50% of metastatic lesions
- triple-phase liver MDCT is the modality of choice for CRC staging and screening for liver metastases.
- CRLM typically appear as hypoattenuating lesions and are best identified in the portal venous phase of scanning but it can miss the lesion less than 1 cm
- MRI superior to CT in detecting and characterising indeterminate small lesions , more accurate in differentiating benign and malignant sub centimetre liver lesions, and more accurate in detecting and characterising CRLM if there is underlying liver parenchymal disease
- PET CT to identify metabolically active metastatic lesions.

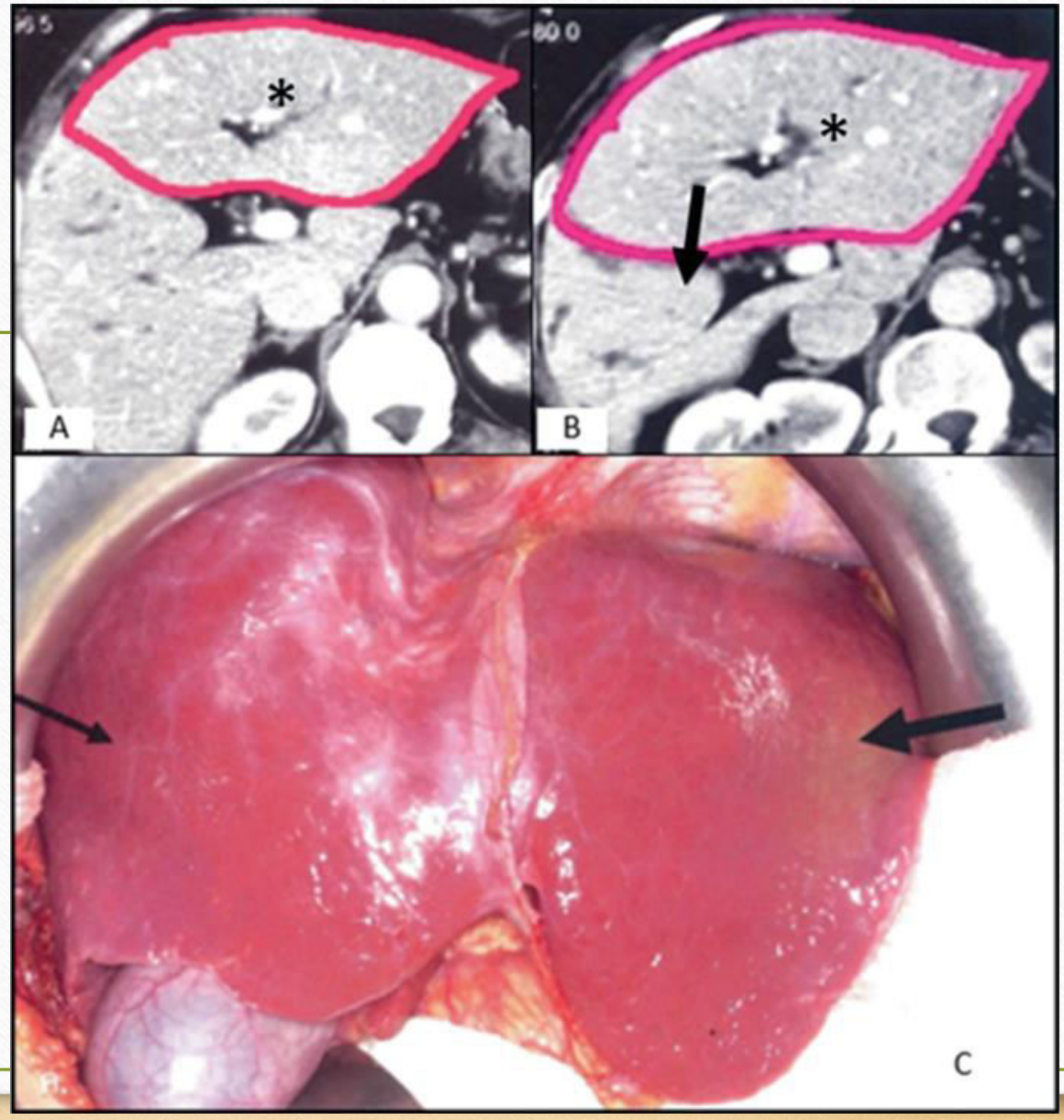


Multiple colorectal cancer liver metastases involving segments VIII, VII, V, VI and IV, with tumor-free left lateral liver lobe

Treatment

- MDT decision should be applied
- Surgical resection with negative microscopic margins (R0 resection) offers patients with CRLM the best chance for long-term survival
- The decision depend on the extent of the liver mets and the presence of primary disease , extra hepatic mest , FLR , prior neo adjuvant chemotherapy, vascular invasion and proximity to the major hepatic vein
- FLR is the future liver remnant post surgery (at least 20% in normal liver , 30% in chronic liver disease and 40 % in cirrhotic liver)
- Other options RFA , chemotherapy




A
B
C

- hepatic resection can be considered in patients with extrahepatic disease amenable to surgical resection or long-term oncologic control with adjuvant chemotherapy.

- In case of small FLR we can used Portal vein embolization of the lobe that have the mets before the surgery to induce atrophy of the affected liver lobe and hypertrophy on the non diseased lobe in effort to have adequate FLR and avoiding the post hepatectomy liver failure

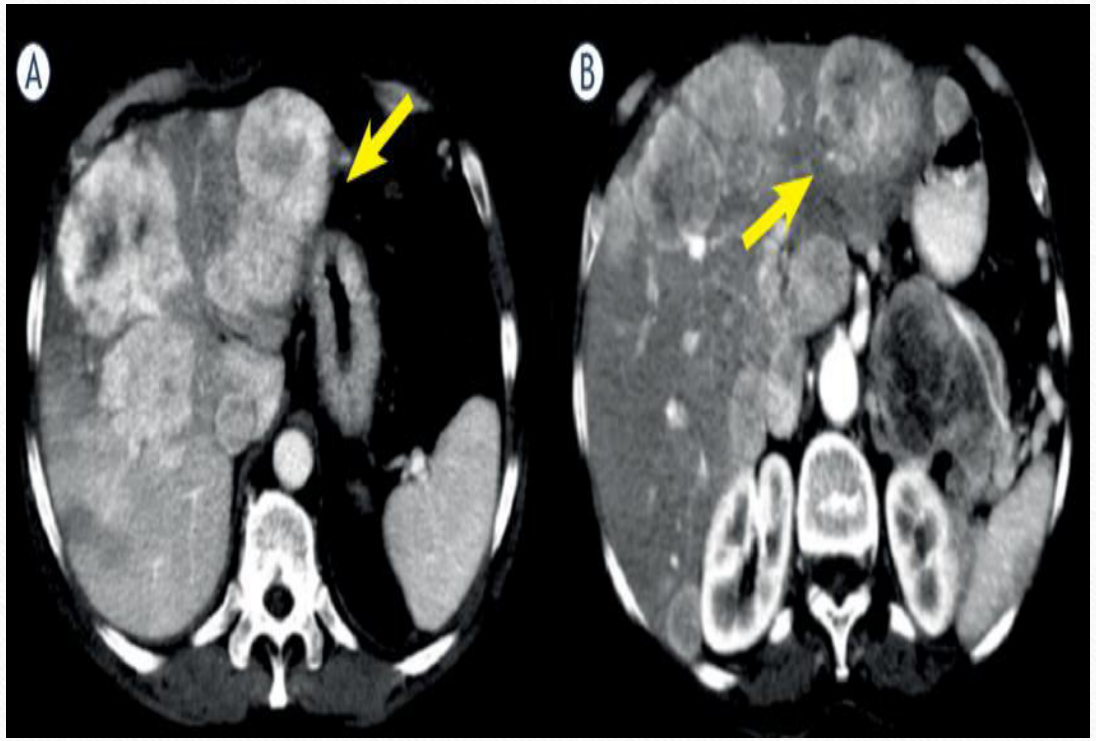
NET
Neuro-endocrine tumour mets

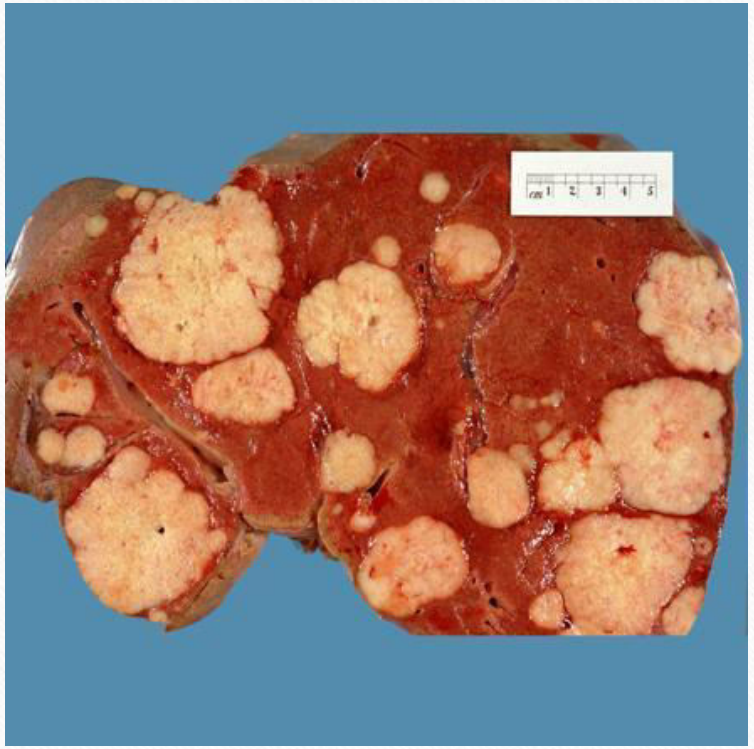
- Either from pancreatic or small bowel origin
- Tend to be large , multifocal and bilobar
- Symptoms related either to the hormonally active disease or pressure symptoms and hepatomegaly
- less than 20% are candidates for surgery
- Liver resection may be performed with curative intent, symptom control or prolongation of survival in the palliative setting.
- Vascularity of the tumour is high

- Diagnosis : Liver triphasic CT , liver MRI
- Overall survival after surgery >80% at 5 years (more than the CRLM or other primary liver tumour)
- Treatment decision depend on the disease extent , symptoms , grade of the tumour
- Surgical treatment with curative intent is the best modality if the patient fit for the surgery and the extent of the disease permit doing safe hepatectomy otherwise cytoreductive surgery is the option for symptomatic control

- Somatostatin analogue used for symptomatic treatment in hormonally active disease
- Other option RFA , TACE , PRRT
- Limited role of systemic chemotherapy

Hyperintense lesion that enhanced on CT with contrast during the arterial phase





Pancreatic malignant tumour

Exocrine :
the most common
Including PDAC , Mucinous , adenosquamous

Endocrine : P-NET -5% of pancreatic tumour (insulinoma , Glucagonoma , Gastrinoma , VIPoma)

Pancreatic malignant tumour

- PC is the seventh leading cause of cancer-related deaths worldwide
- The annual incidence rate worldwide for all histologic types of pancreatic cancer is approximately 4.9 new cases per 100,000 persons, ranking 12th among all cancers globally
- In Jordan 3.7 new case per 100,00 person

PDAC

- Pancreatic ductal adenocarcinoma (PDAC) is most common pancreatic cancer and the most common exocrine pancreatic cancer
- MC site: Head (75%) > Body (15%) >Tail (10%)
- More common in Men, African Americans, mean age at diagnosis is 72 years

Clinical presentation

- MC symptom for patients with PDACs in the periampullary region is jaundice which could be painless or painful
- Pain typically arising in epigastrium & radiating to the back.
- Weight loss affecting more than 50% of individuals.
- For tumours of body & tail of pancreas, pain & weight loss become more common at presentation.
- A palpable distended gallbladder in 1/3rd of patients with periampullary PDAC (Courvoisier sign)
- With widespread disease, a left supraclavicular node (Virchow's node)may be palpable. Periumbilical lymphadenopathy may be palpable (Sister Mary Joseph's node)

Cont.. Clinical presentation

- vomiting reflecting gastric outlet obstruction,
- peripheral migratory venous thrombosis (Trousseau's sign)
- pancreatitis in the absence of other potential precipitants such as gallstones or regular alcohol use
- pancreatic insufficiency (either exocrine and/or endocrine) ie: Late-onset diabetes Signs of malabsorption without defined cause

- **Association** between risk of **pancreatic cancer**, **H. pylori** colonization, and **ABO** blood groups
- **Established risk factors**: **Smoking (Tobacco)** and **Inherited susceptibility**[Q]

- **K-ras2** oncogene is **activated** (by point mutation) in **>95%** of pancreatic cancers (**MC gene mutation**)[Q]

Risk factor

Box 16.1 • Risk factors for pancreatic cancer

- Age (above 60 years)
- Smoking
- Obesity
- High fat diet
- Alcohol abuse
- Pancreatitis
  - Chronic pancreatitis
  - Hereditary pancreatitis
- Diabetes mellitus
- Family history of pancreatic cancer
- Genetic predisposition
  - Peutz–Jeghers syndrome
  - Li–Fraumeni syndrome
  - Fanconi syndrome
  - Familial adenomatous polyposis
  - Lynch syndrome
  - Gardner syndrome
  - Multiple endocrine neoplasia
  - *BRCA1*
  - Von Hippel–Lindau syndrome

Investigation

Blood test

largely unhelpful in diagnosis(normochromic anaemia, raised bilirubin and ALP , amylase and lipase may be elevated in those presenting with pancreatitis (5%)

TM –Ca19.9

CA 19-9 has suboptimal sensitivity (41–86%) and specificity (33–100%) for detecting pancreatic cancer

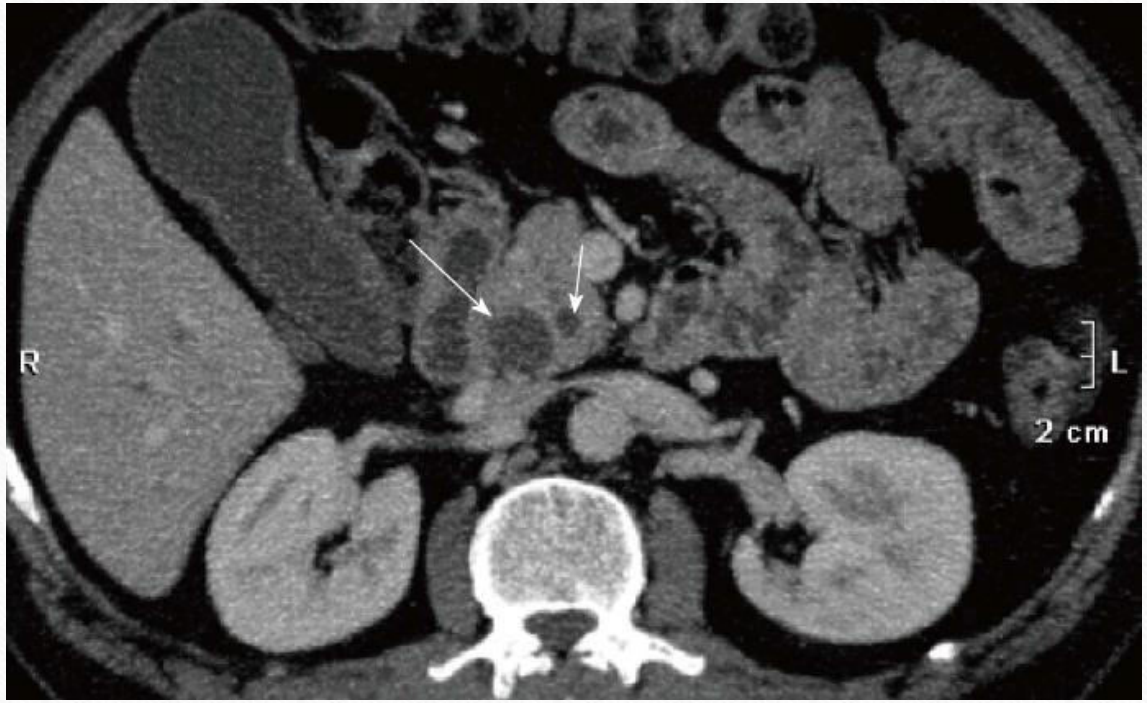
4–15% of the general population do not express the antigen and hence do not have detectable serum CA 19-9 levels

Ca19.19 Can be elevated in benign condition like cholecystitis , cholangitis , chronic pancreatitis

Cont .. Investigation

- because of these limitations, CA 19-9 is mostly used as a prognostic marker to assess response to therapy in patients already diagnosed with pancreatic cancer
- US : Initial modality in jaundice patient looking for other cause (CBD stone), dilated CBD , ascites , liver mets
- CT- pancreas , more sensitive than the US , investigation of choice for the evaluation of lesions arising in the pancreas

- CT shows the pancreatic mass site , any evidence of vascular invasion to SMA, SMV-PV , liver and extra-abdominal mets , assessment of the resectability
- Signs on CT : hypointense mass
- double ductal Sign (dilated CBD &PD) on CT scan is on the the sign of pancreatic cancer on the CT but in general this sign is seen more commonly with ampullary tumour


R
L
2 cm

Investigations

EUS: For identifying lesions that do not appear on CT and in case if we need to have a biopsy

Tissue diagnosis is not necessary prior to routine resection unless the patient planned to have the chemotherapy in this case biopsy is required

Magnetic resonance imaging (MRI) is mainly used as an adjunct to CT for planning treatment options

PET-CT scanners are able to detect small (up to 7mm) pancreatic neoplasms and diagnose metastatic

Staging

Don't memorize it

TNM CLASSIFICATION OF PANCREATIC CANCER

8th AJCC (2017) TNM Classification of Pancreatic Cancer	
Tis	Carcinoma in situ
T1	Tumor limited to pancreas **upto 2 cm** in greatest dimension
	T1a: Tumor **≤0.5 cm** in greatest dimension
	T1b: Tumor **>0.5 cm** but **≤1 cm** in greatest dimension
	T1c: Tumor **>1 cm** but **≤2 cm** in greatest dimension
T2	Tumor limited to pancreas **>2-4 cm** in greatest dimension
T3	Tumor **>4 cm** in greatest dimension
T4	Tumor involves **celiac axis**, **superior mesenteric artery** and/or **common hepatic artery**
N1	Metastasis in **1-3** regional LN
N2	Metastasis in **4 or more** regional LN
M1	Distant metastasis

Stage 0	Stage IA	Stage IB	Stage IIA	Stage IIB	Stage III	Stage IV
Tis N0 M0	**T1** N0 M0	**T2** N0 M0	**T3** N0 M0	**T1-T3 N1** M0	**T1-T3 N2** M0 **T4** AnyN M0	Any T AnyN **M1**

Treatment

- MDT
- Assessment if the tumour is resctable
- Palliative option ?
- Role of ERCP and stenting in jaundice patient: pre op , or palliative or if the patient planned for neoadjuvant chemotherapy
- Symptoms of GOO
- Only 20 % are surgically resctable at the time of diagnosis

TABLE 62.2 National Comprehensive Cancer Network® (NCCN®) Criteria Defining Resectability Status

Resectability Status	Arterial	Venous
Resectable	No arterial tumor contact with CA, SMA, or CHA	No tumor contact with SMV or PV or ≤180-degree contact without vein contour irregularity
Borderline resectable	*Head/uncinate process* • Solid tumor contact with the SMA of ≤180 degree • Solid tumor contact with the CHA without extension to CA or bifurcation of the hepatic artery to allow safe and complete resection and reconstruction • Presence of variant arterial anatomy (ex: accessory right hepatic artery, replaced right hepatic artery, replaced CHA and the origin of replaced or accessory artery) and the presence and degree of tumor contact should be noted if present as it may affect surgical planning. *Body/tail* • Solid tumor contact with the CA ≤180 degrees • Solid tumor contact with the CA of >180 degrees without involvement of the aorta and with intact and uninvolved gastroduodenal artery	Solid tumor contact with the SMV or PV of >180 degrees, contact of ≤180 degrees with contour irregularity of the vein, or thrombosis of the vein but with suitable vessel proximal and distal to the site of involvement allowing safe and complete resection with reconstruction Solid tumor contact with the IVC
Unresectable	Distant metastasis (including non-regional lymph node metastasis) *Head/uncinate process* • Solid tumor contact with SMA >180 degrees • Solid tumor contact with CA >180 degrees • Solid tumor contact with first jejunal SMA branch *Body/tail* • Solid tumor contact of >180 degrees with the SMA or CA • Solid tumor contact with the CA and aortic involvement	*Head/uncinate process* • Unreconstructible SMV/PV due to tumor involvement or occlusion • Contact with the most proximal draining jejunal branch into SMV *Body/tail* • Unreconstructible SMV/PV due to tumor involvement or occlusion

CA, Celiac axis; *CHA*, common hepatic artery; *IVC*, inferior vena cava; *PHA*, proper hepatic artery; *PV*, portal vein; *RHA*, right hepatic artery; *SMA*, superior mesenteric artery; *SMV*, superior mesenteric vein.

Don't memorize this table –its beyond your level just note the highlight items to understand the management

- Criteria to assess if the tumour is resectable , borderline resecatble or unresectable

Resectable

- Surgical resection remains the only potentially curative treatment of pancreas cancer if the patient fit to go for it
- Tumours of head of the pancreas(Whipples –classical or PPPD)
- Tumours of body & tail of the pancreas-Distal pancreatectomy and en-bloc splenectomy
- In addition, post operative adjuvant chemotherapy .

Borderline resectable

- Neo adjuvant chemotherapy
- Then re assessment if become resecatble after the chemotherapy we will follow the same treatment plan of the resectable cancer
- If not we will go for palliative treatment

Unresectable palliative

- Palliative chemotherapy
- Symptomatic management of pain , jaundice and GOO as shown in the table :

Palliative Therapy for Pancreatic Cancer	
• Biliary obstruction	• **ERCP** with **metal stent placement** (**Best**)[Q] • Roux-en-Y hepaticojejunostomy
• Gastric outlet obstruction	• **Endoscopic stenting** (**Preferred**)[Q] • Double bypass (Roux-en-Y hepaticojejunostomy + gastrojejunostomy)
• Pain	• **NSAIDs** or **opiates**[Q] • **Celiac nerve block**[Q]

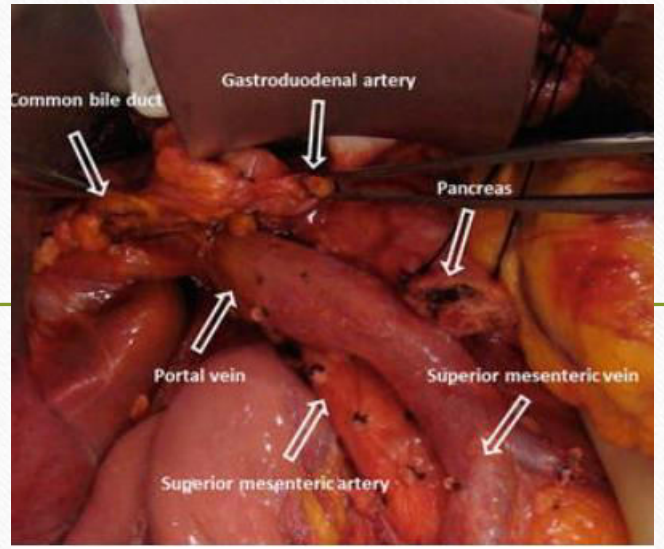
Prognosis

- Five-year survival after curative resection (pancreaticoduodenectomy) approaches 15-20 %

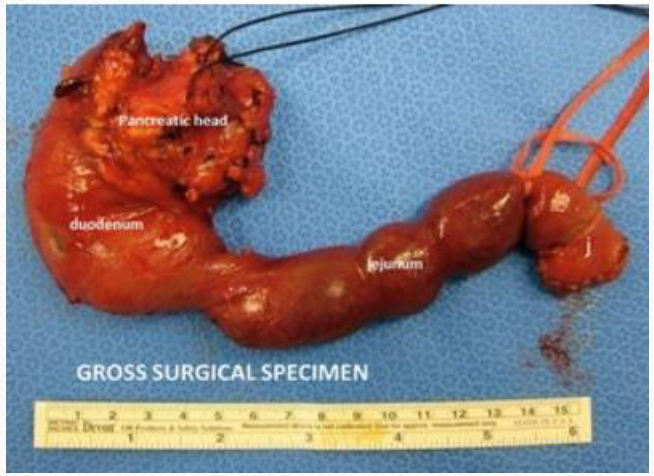
Median Survival in Carcinoma Pancreas	
• **Resectable** disease (stage **I** and **II**)	• **15-20** months[9]
• **Locally advanced** disease (stage **III**)	• **6-10** months[9]
• **Metastatic** disease (stage **IV**)	• **3-6** months[9]

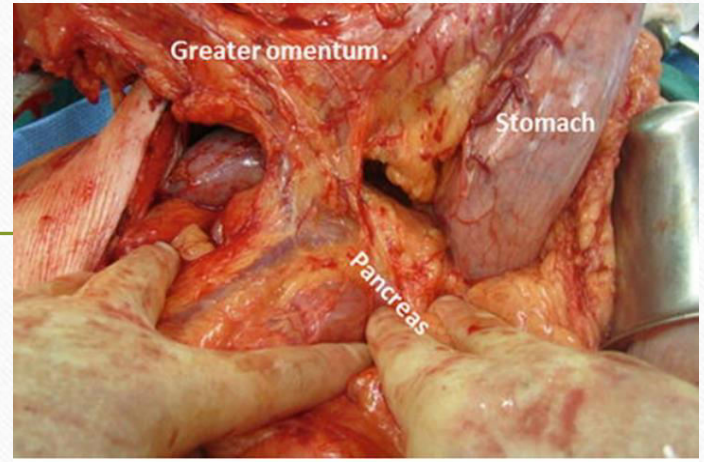
Whipple's Procedure Involves Resection of	
• Distal stomach[Q] • Gallbladder[Q] • CBD[Q] • Head of pancreas[Q]	• Duodenum[Q] • Proximal jejunum[Q] • Regional lymphatics

Restoration of GI Continuity Requires		
• **Pancreaticojejunostomy[Q]**	• **Hepaticojejunostomy[Q]**	• **Gastrojejunostomy[Q]**

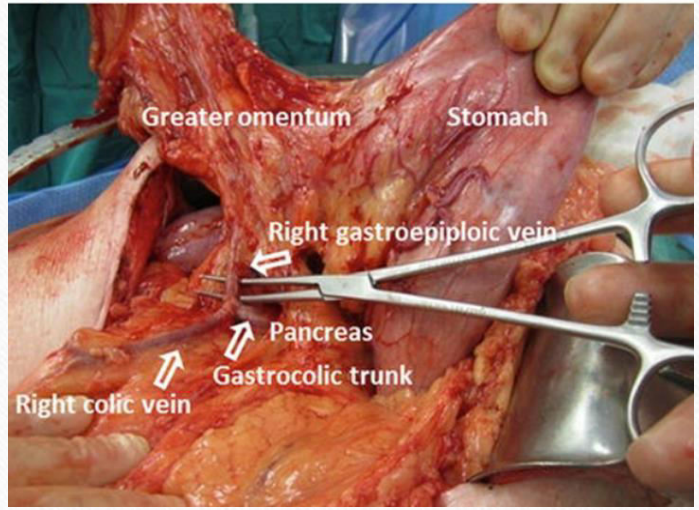


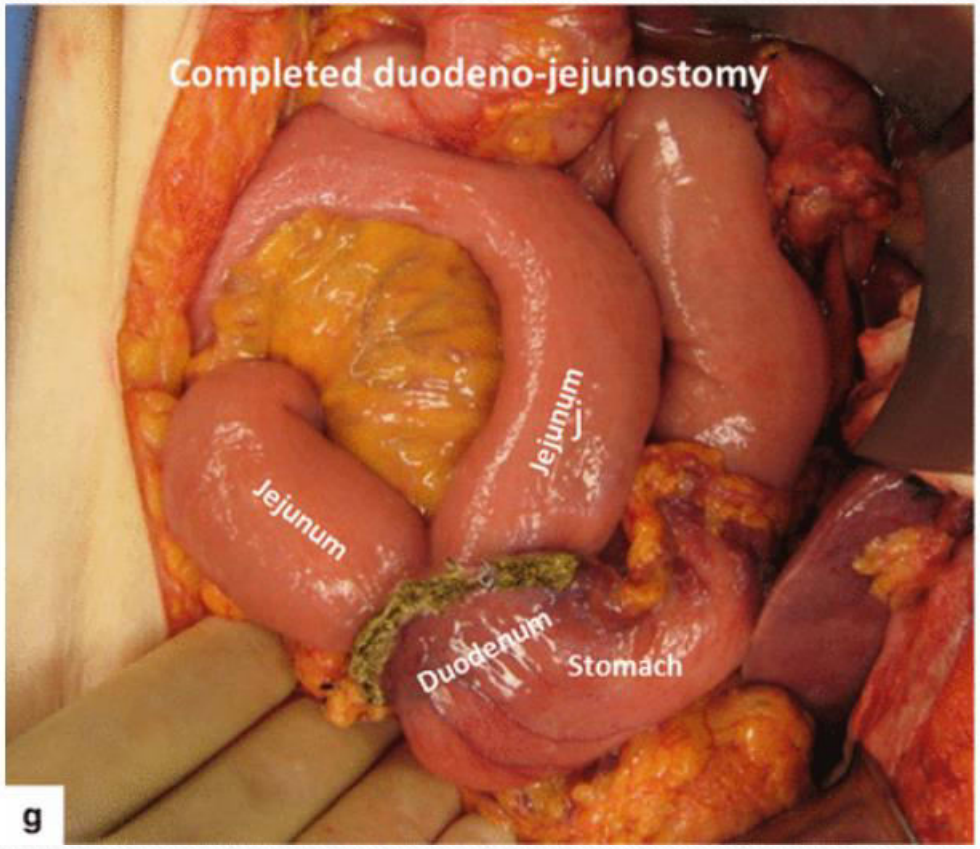
Figs. 19.16
Transected CBD

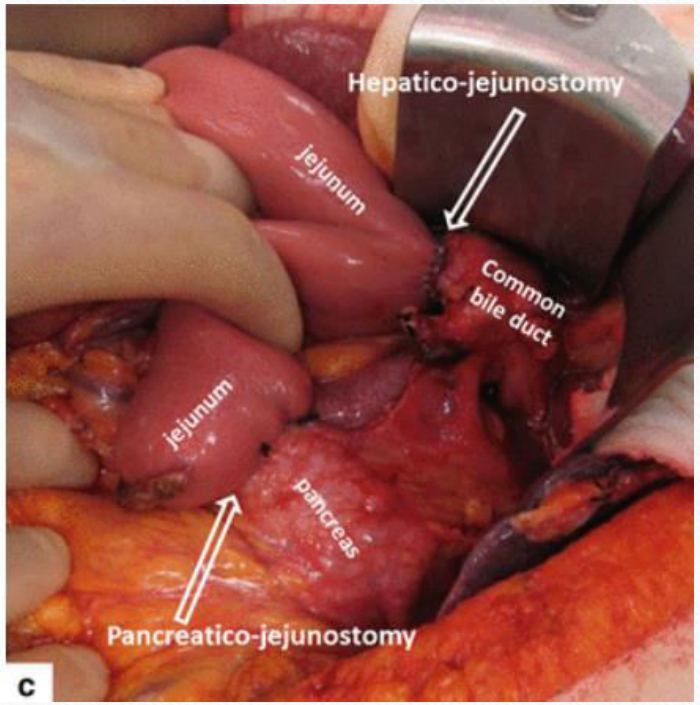




s. 19.4
tering the lesser sac




Completed duodeno-jejunostomy
Jejunum
Jejunum
Duodenum
Stomach
g


Hepatico-jejunostomy
Jejunum
Common bile duct
Jejunum
Pancreas
Pancreatico-jejunostomy
c

P-NET

Non functional (most common)

Functional

Insulinoma is the most common functional P-NET

Gastrinoma is the most common malignant functional P-NET

functional tumors are associated with better survival than nonfunctional PNETs because they are more often identified at an earlier stage

Low- and intermediate-grade (G1 and G2, respectively) PNETs have significantly better 5-year OS (75% and 63%, respectively) than do G3 tumors (7%)

TABLE 65.1 Grading System for Pancreatic Neuroendocrine Tumors[1]

TERMINOLOGY	DIFFERENTIATION	GRADE	MITOTIC RATE (mitoses/2 mm^2)	Ki-67 INDEX (PERCENT)
NET, G1	Well differentiated	Low	<2	<3
NET, G2	Well differentiated	Intermediate	2 to 20	3 to 20
NET, G3	Well differentiated	High	>20	>20
NEC (small cell or non-small cell)	Poorly differentiated	High	>20	>20

Insulinoma

- The average age at diagnosis is 45 years, Typically small
- 97% in pancreas (equal distribution in the head, body, and tail)
- 3% in duodenum, splenic hilum, or gastrocolic ligament
- Diagnostic hallmark is Whipple's triad: Fasting-induced neuroglyopenic symptoms of hypoglycemia (diaphoresis, shaking, mental confusion, obtundation, and seizures), low blood glucose levels (40 to 50 mg/dL), and relief of symptoms after the administration of glucose
- Significant weight gain: Patients eat frequently to prevent hypoglycemia.
- It is a painless condition
- Sporadic in majority of the cases

- Gold standard test for the diagnosis of insulinoma is the 72-hour fasting test
- An insulin-to-glucose ratio > 0.4 is consistent with insulinoma
- CECT or MRI: Hyperattenuating
- Portal venous sampling for insulin with or without arterial stimulation with calcium is the best pre-operative method of localization
- Treatment
- 1- Diazoxide decreases beta cell release of insulin
- 2- surgery

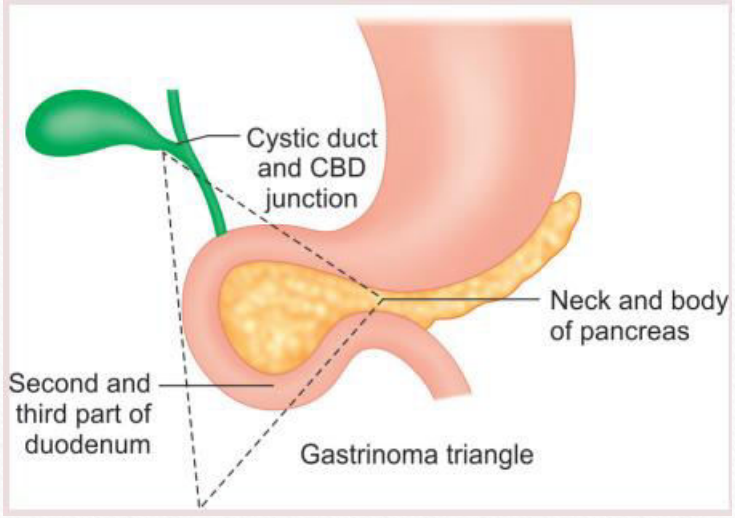
GASTRINOMA/ZOLLINGER-ELLISON SYNDROME

- Gastrinoma is MC functioning malignant pancreatic endocrine tumor. •
- More common in men, mean age 50 years
- • ZES occur in two forms: Sporadic (75%) & MEN-1 association (25%)
- • Those associated with MEN-1 are almost always multiple, early onset, more common in duodenum
- MC site is duodenum (50-70%) followed by Pancreas (20-40%)

- • About 70-90% of gastrinomas are located within the Passaro's triangle

Boundaries of Passaro's Triangle

- Junction of cystic duct and CBD[Q]
- Junction of 2nd & 3rd part of duodenum[Q]
- Junction of neck & body of pancreas



Clinical Features

- • Gastric acid hypersecretion causes peptic ulcer disease often refractory severe diarrhea
- MC presenting symptoms are abdominal pain(70-100%), diarrhea (50-70%) & GERD (30-35%)
- 100% patients will have a fasting serum gastrin level >100 pg/mL
- If the diagnosis is in doubt, the provocative tests are highly useful: • Secretin Provocation Test: An increase of >200 pg/mL in the gastrin value after administration of secretin is diagnostic

- Somatostatin receptor scintigraphy (SRS) is imaging test of choice for localizing both primary and metastatic gastrinomas
- Treatment : PPI +Surgery depending on the location
- Consider genetic testing in those whom MEN1 is suspected with consideration to rule out parathyroid adenoma and pituitary adenoma

Glucagonoma

- More common in females; 70% are malignant
- MC site: Body and tail of pancreas.
- Classic presentation of the 4Ds: Diabetes, dermatitis, DVT, and depression
- Fasting glucagon level >50 pmol/L is considered diagnostic + CT scan
- Necrolytic erythema migrans are MC manifestations of the disease, seen in 2/3rd of patients
- Resection is the treatment of choice

VIPomas (Verner-Morrison Syndrome)

- Also known as WDHA syndrome (watery diarrhea, hypokalemia, achlorhydria) or pancreatic cholera
- Usually solitary; MC site is tail of pancreas, Two-thirds are malignant
- Diagnostic triad: Secretary diarrhea + High levels of circulating VIP + Pancreatic tumor
- Profuse, watery, iso-osmotic secretary diarrhea is MC presenting symptom
- Treatment :
- preoperative hydration and correction of electrolyte abnormalities & Octreotide
- Resection is the treatment of choice

Precursor lesions

- These precursor lesions include:

1- pancreatic intraepithelial neoplasia (PanIN)(the commonest)

2- intraductal papillary mucinous neoplasm (IPMN)

3- mucinous cystic neoplasm (MCN).

We will speak only about 2& 3

IPMN
Intraductal Papillary Mucinous Neoplasm

- IPMN is also known as mucin-secreting carcinoma, villous adenoma of the duct of Wirsung
- Seen in 6th to 7th decade of life; Equal sex distribution
- • More common in head & uncinate process of the pancreas
- **Types of IPMN**
- – Side branch IPMN: Involves dilation of the pancreatic duct side branches
- – Main duct IPMN: Abnormal cystic dilation of the main pancreatic duct
- – Mixed-type IPMN: Side branch IPMN that has extended to involve the main pancreatic duct

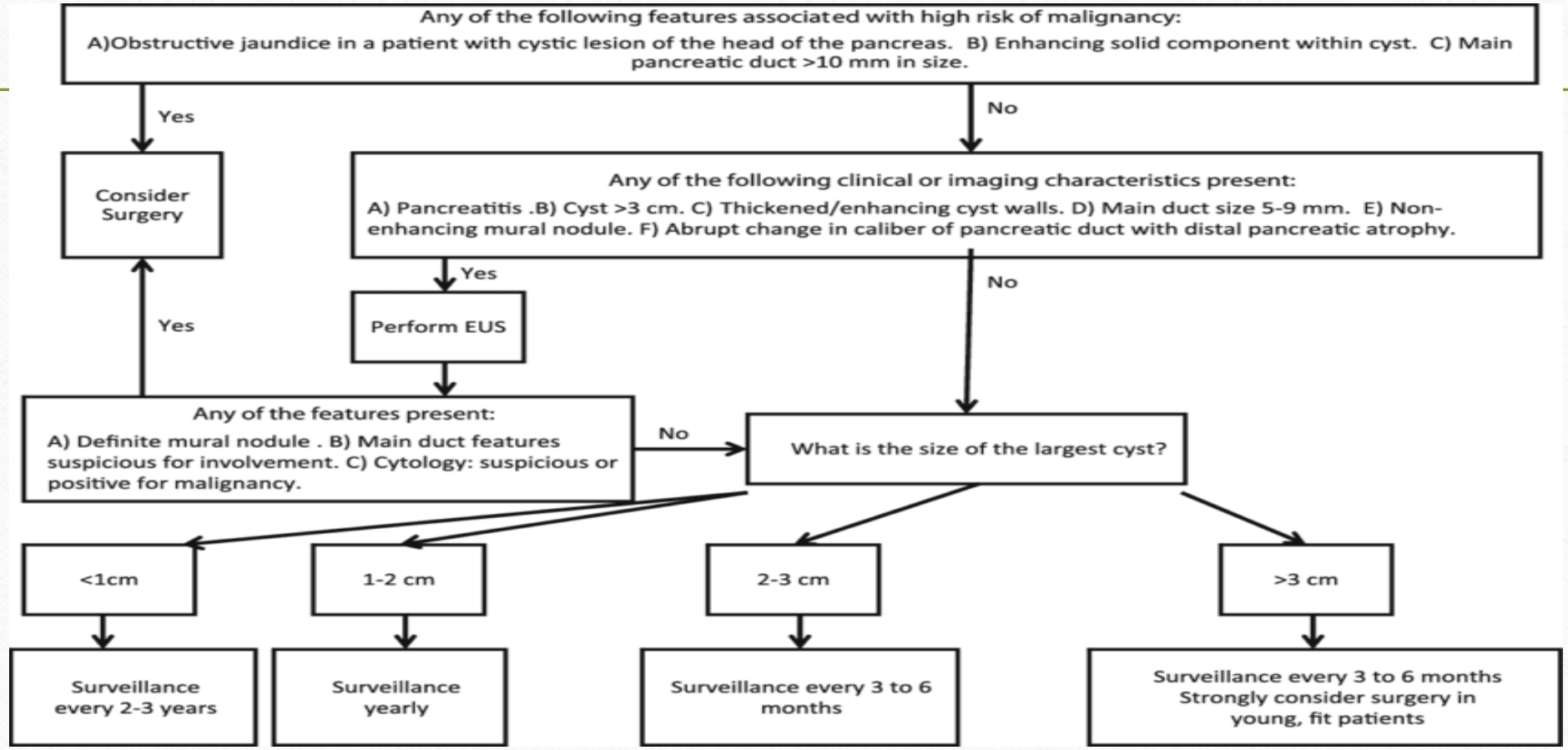
Clinical Features

- abdominal pain or recurrent pancreatitis, (caused by obstruction of pancreatic duct by thick mucin
- 5-10% have steatorrhea, diabetes, & weight loss secondary to pancreatic insufficiency.
- • Careful histologic examination of the entire specimen (invasive component in (36%–100%)in Main duct type and 12-30% in branch type

Diagnosis

- Endoscopy: Mucus extruding through a large, fish-mouth like papillary orifice is virtually diagnostic of IPMN
- CT scans: Dilated main pancreatic duct, cysts of varying sizes, and possibly mural nodules
- Aspirated fluid: Mucinous content with elevated CEA & amylase level
- Pancreatic resection is the standard treatment for MCNs

Treatment


Any of the following features associated with high risk of malignancy:
A)Obstructive jaundice in a patient with cystic lesion of the head of the pancreas. B) Enhancing solid component within cyst. C) Main pancreatic duct >10 mm in size.
Yes
No
Consider Surgery
Any of the following clinical or imaging characteristics present:
A) Pancreatitis .B) Cyst >3 cm. C) Thickened/enhancing cyst walls. D) Main duct size 5-9 mm. E) Non-enhancing mural nodule. F) Abrupt change in caliber of pancreatic duct with distal pancreatic atrophy.
Yes
No
Yes
Perform EUS
Any of the features present:
A) Definite mural nodule . B) Main duct features suspicious for involvement. C) Cytology: suspicious or positive for malignancy.
No
What is the size of the largest cyst?
<1cm
1-2 cm
2-3 cm
>3 cm
Surveillance every 2-3 years
Surveillance yearly
Surveillance every 3 to 6 months
Surveillance every 3 to 6 months
Strongly consider surgery in young, fit patients

Mucinous Cystadenoma of Pancreas

- Most Common cystic neoplasm of the pancreas
- Frequently seen in young women, mean age 5th decade
- More common in the body & tail of the pancreas
- almost exclusively found in females
- ovarian-like stroma surrounding the columnar epithelium is considered a pathognomonic finding
- Risk of invasive carcinoma 10-50 %

- CT scan: Presence of a solitary cyst with fine septations & rim of calcification
- Cyst fluid analyses: Mucin-rich aspirate, high CEA & low amylase levels

Thank you