Liver abscesses and cystic liver diseases

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Project ECHO®
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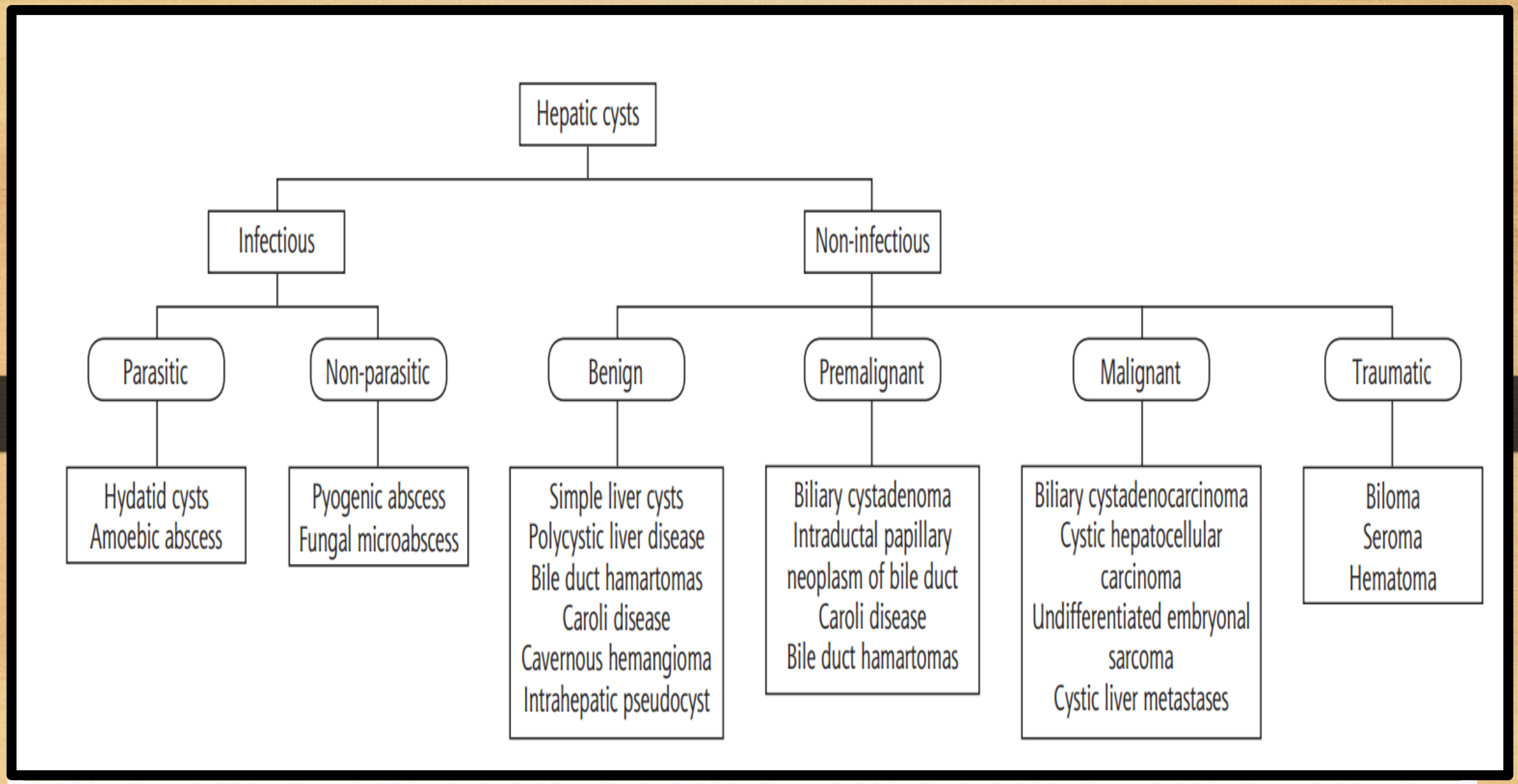
Cystic Liver Diseases

Introduction

- **Heterogeneous lesions**
- **Prevalence** (15-18% in the US)
- Most detected incidentally on imaging
- **Vary** – Pathogenesis/Clinical presentation/Radiological
- **Symptomatic** (10-15%)
- **Benign > Malignant**
- **Simple cysts** – 2.5-18%
- **Congenital cysts** – female predominance (40-70yrs)
- **Acquired cysts** – male predominance (30-50yrs)



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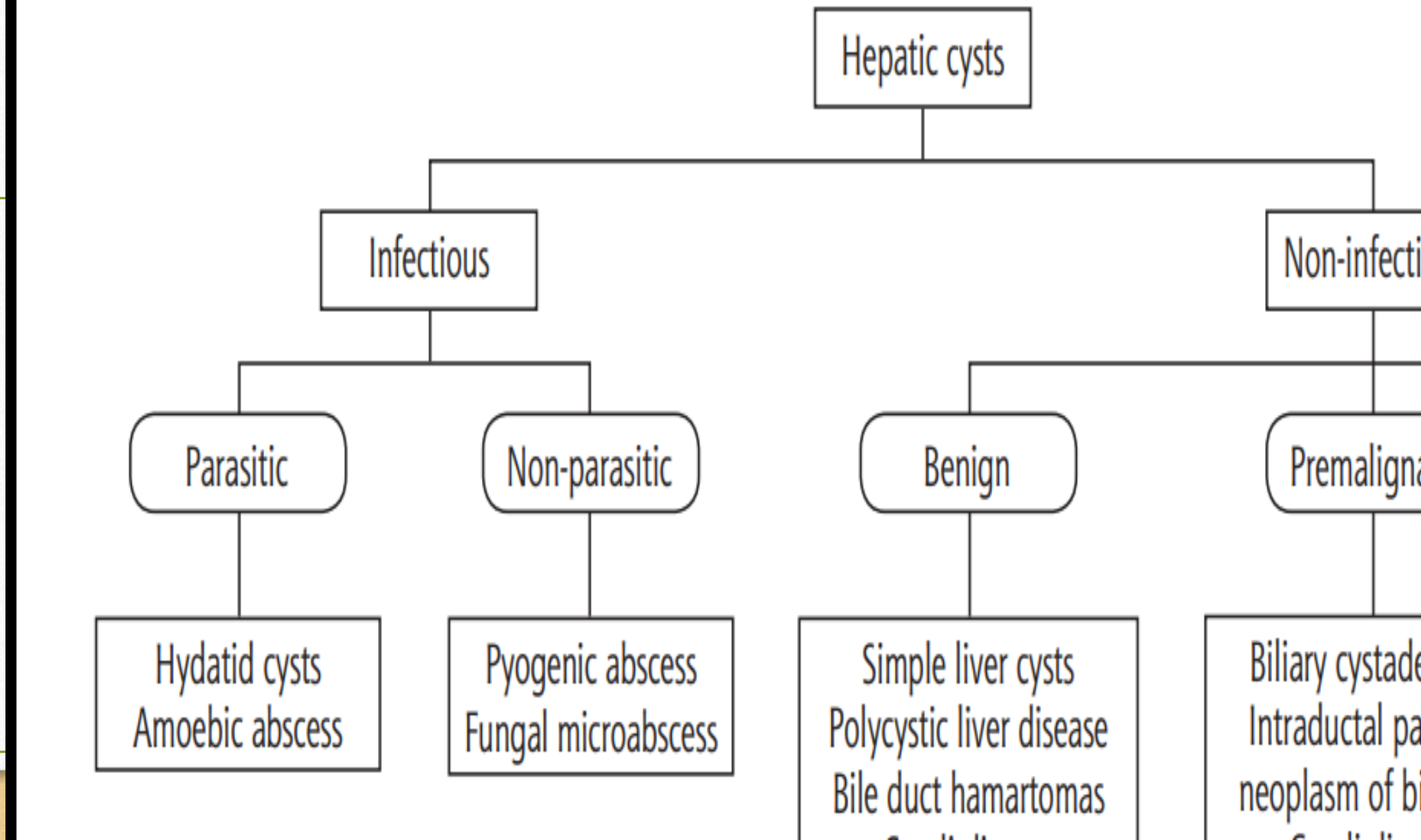
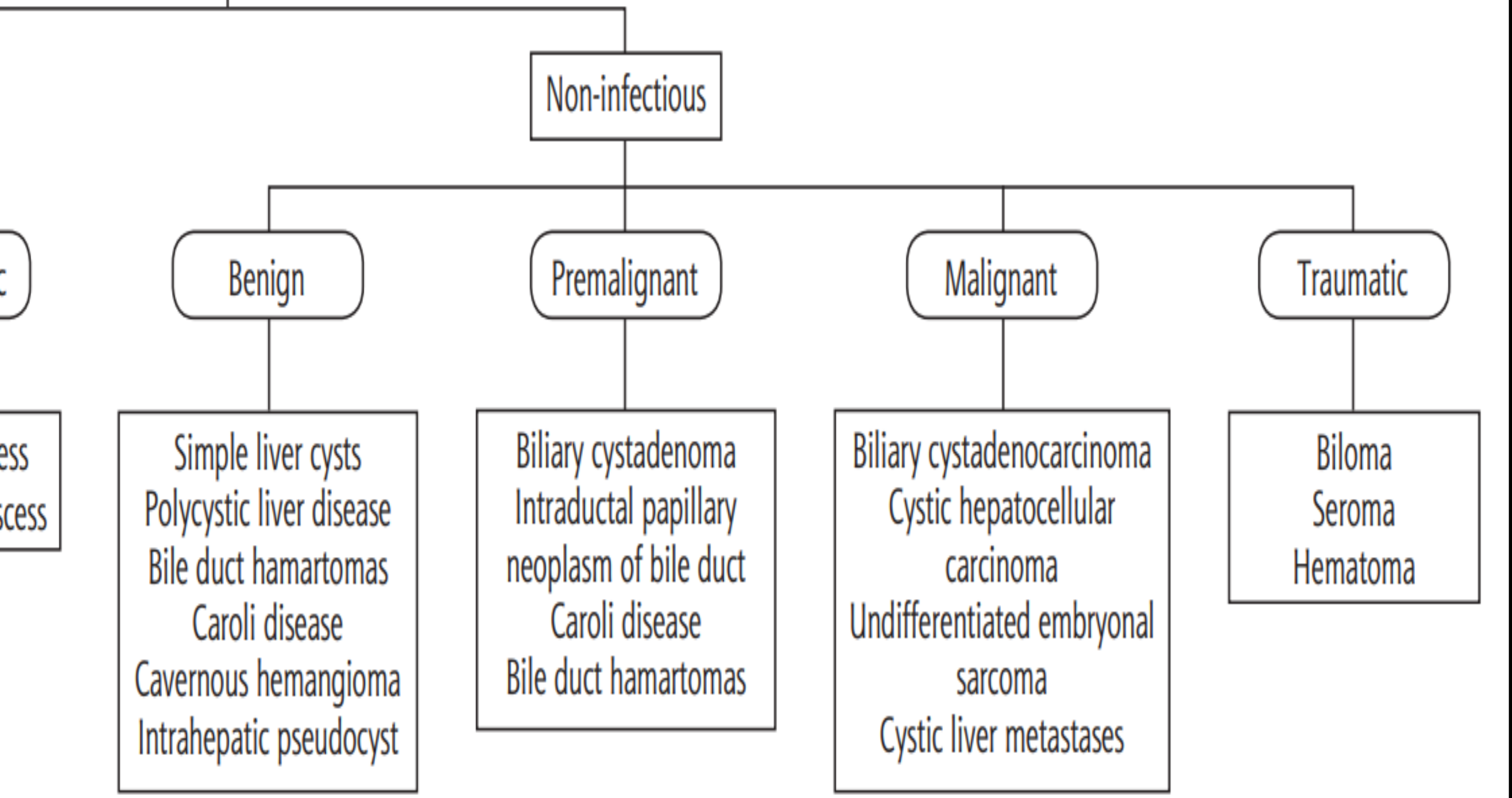

Hepatic cysts
Infectious
Non-infecti
Parasitic
Non-parasitic
Benign
Premaligna
Hydatid cysts
Amoebic abscess
Pyogenic abscess
Fungal microabscess
Simple liver cysts
Polycystic liver disease
Bile duct hamartomas
Biliary cystade
Intraductal pa
neoplasm of bi


Non-infectious
Benign
Premalignant
Malignant
Traumatic
Simple liver cysts
Polycystic liver disease
Bile duct hamartomas
Caroli disease
Cavernous hemangioma
Intrahepatic pseudocyst
Biliary cystadenoma
Intraductal papillary
neoplasm of bile duct
Caroli disease
Bile duct hamartomas
Biliary cystadenocarcinoma
Cystic hepatocellular
carcinoma
Undifferentiated embryonal
sarcoma
Cystic liver metastases
Biloma
Seroma
Hematoma

- **Hepatic Cysts** - fluid-filled lesions lined by a single cell layer.
  - Hepatic parenchyma
  - Biliary tract
- **Three main types**:
  1. Fibrocystic liver disorders
  2. Mucinous cystic neoplasms (MCN), Previously cystadenomas and cystadenocarcinomas
  3. Hydatid cysts

Fibrocystic liver disorders

1. Simple cyst
2. Polycystic liver disease
3. Fibrocystic diseases associated with ARPKD
4. Von Meyenburg Complexes (Biliary Hamartomas)
5. Caroli's Disease (Type V Choledochal cysts)
6. Congenital hepatic fibrosis
7. Type IV choledochal cysts

Simple Cysts

- Congenital
- Most common benign cyst (2.5%)
- F>M (1.5:1) – 50yrs
- Aberrant bile ducts - no communication with intrahepatic biliary tree
  - Continue to secrete intraluminal fluid
- Usually asymptomatic - <3cm, solitary or multiple <3 (>10 PCLD)
- Single layer of cuboid or columnar epithelial cells
  - Up to 2 septa
- Symptomatic/Complicated – complications
  - Infection, intracystic bleeding, rupture – RARE >10cm (trauma) – infective/hemorrhage/trauma/intervention
  - Compression of adjacent organs – BILE DUCTS (SEGMENT IV)

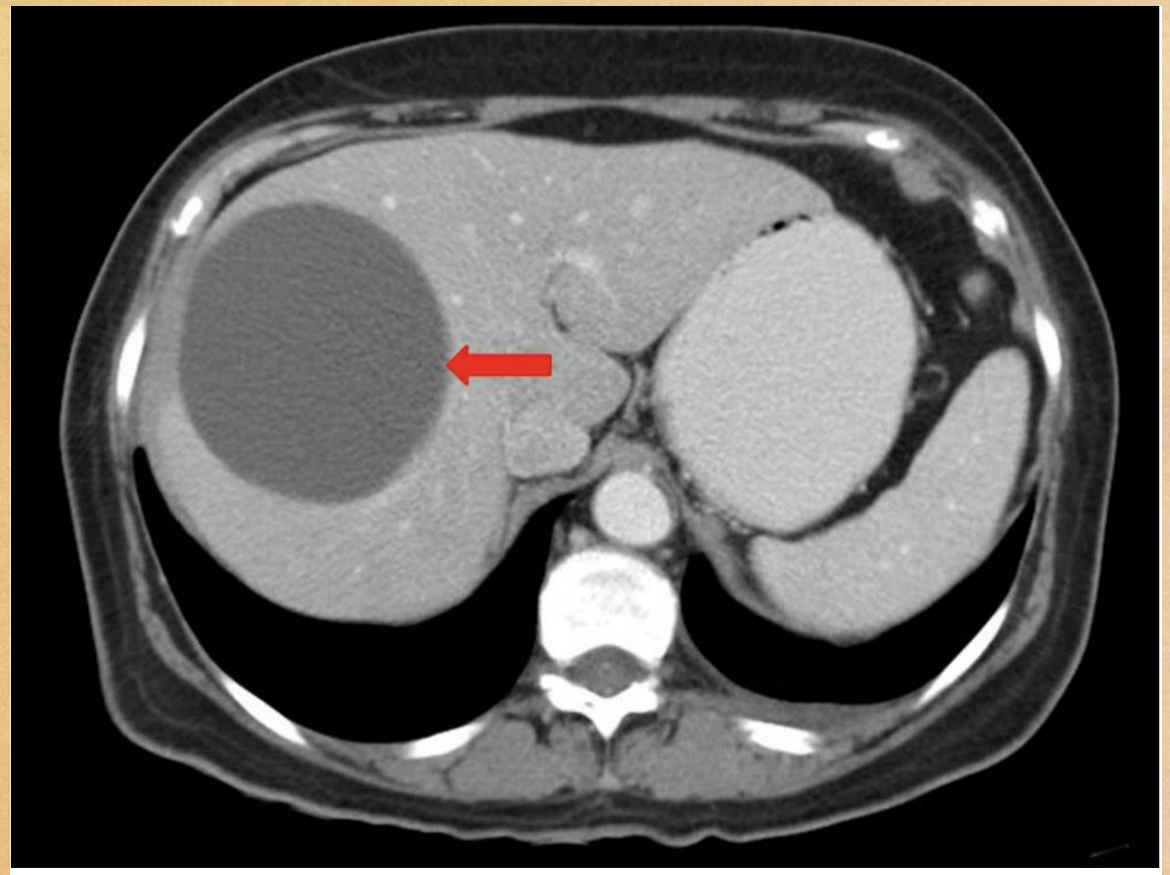


Fig. 1: Contrast enhanced abdominal CT showing a simple hepatic cyst (arrow).

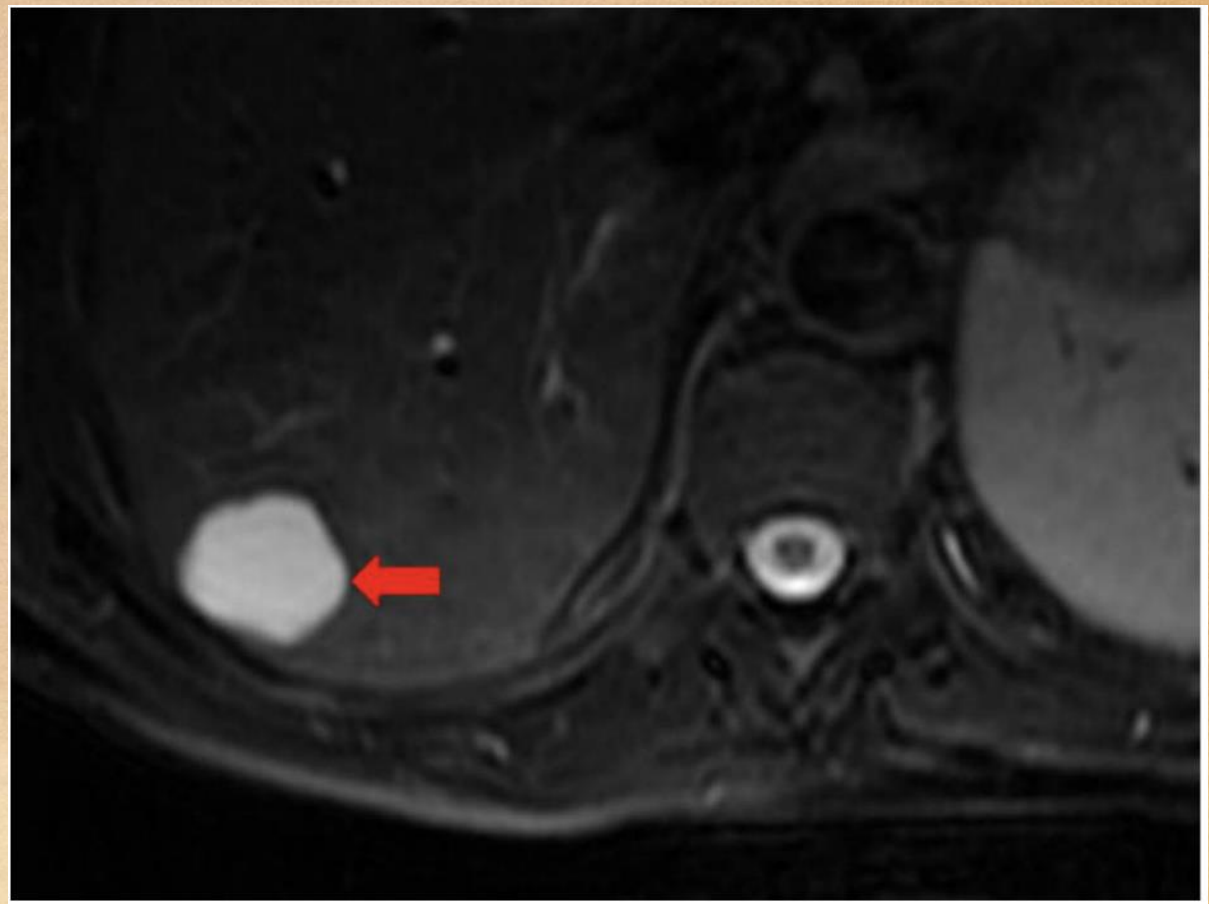


Fig. 2: Axial T2-weighted MR image showing a simple hepatic cyst (arrow).

Diagnosis

- **Ultrasound is the best imaging modality**
  - asymptomatic (left alone)
  - No follow-up indicated
- **CT/MRI** – COMPLICATED CYSTS – intervention/surveillance
- **CEA/CA19.9** (serum/cyst aspirate) – no diagnostic value
- **Tumour-associated glycoprotein72 (TAG72)** – Simple vs MCN
  - >25U/ml (Sen:79% & Spec:97%)

Management

- **Symptomatic:** Volume reducing therapies
- **Percutaneous aspiration sclerotherapy(Recurrence-higher)**
  - 100% ethanol/20% saline/Tetracycline/Polidocanol
  - Symptom relief (76-100%) and resolution (56-100%). Up to 6/12 to work
  - Etoh intoxication and local pain – long duration and high volume etoh use (<1hr)
  - C/I – Fistula/Intracystic haemorrhage
- **Cyst fenestration- Laparoscopy + drainage +cyst wall excision**
  - Recurrence <8%
- **Partial hepatectomy and fenestration- Multiple/Large**
  - Perioperative mortality (14%)
  - Liver failure- mean 6-8 years with need for liver transplant (2-3%)

Cyst haemorrhage

- **Most frequent**- injury to fragile blood vessels of the cyst wall lining
  - >8cm
  - Spontaneously/intervention/rupture
- **Sudden severe pain (80% of patients)** – resolves within few days
- **Localized pain** – resolves within days to weeks
- Unlikely to cause haemodynamic instability/Hb drop

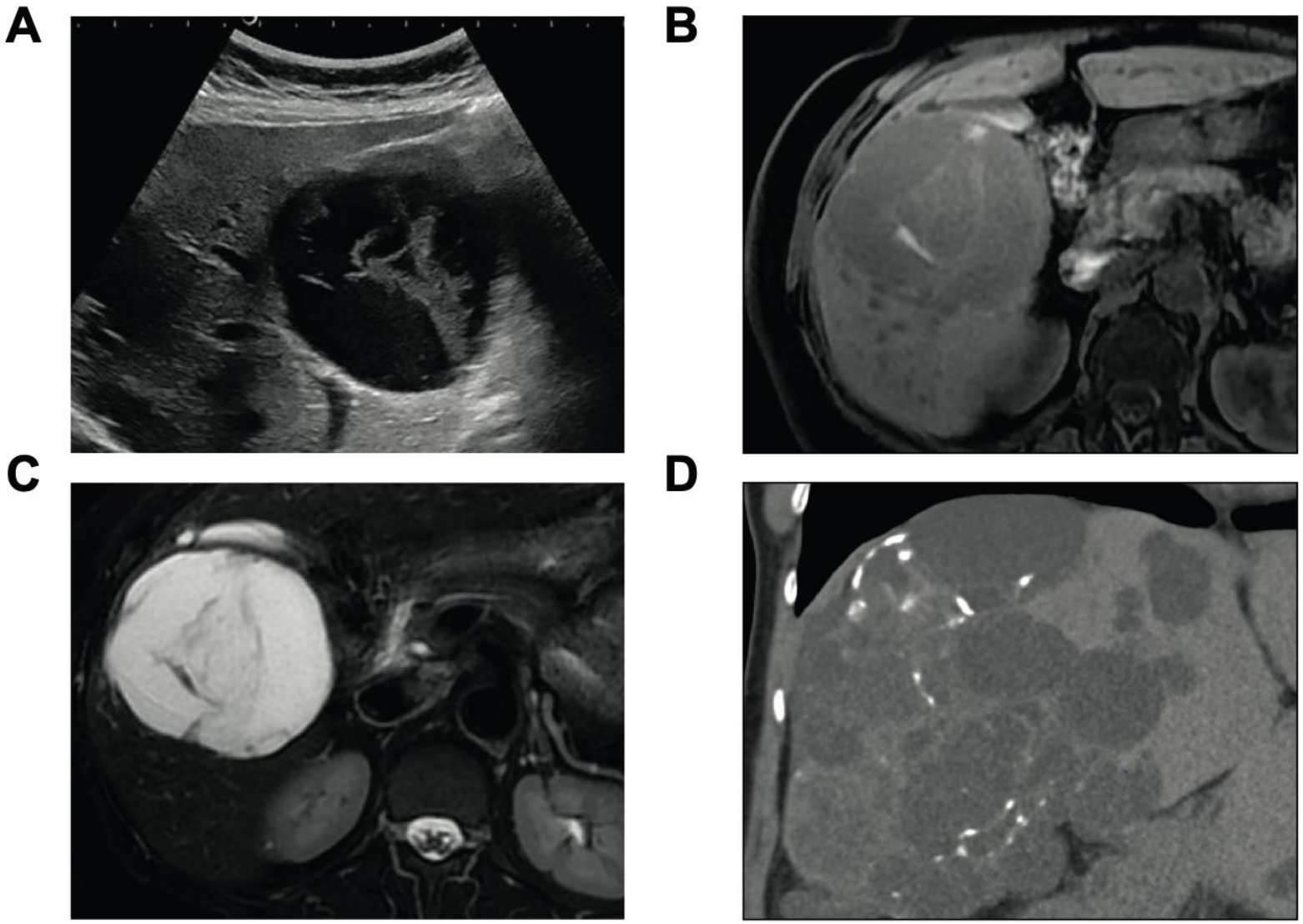


Fig. 2. Haemorrhagic hepatic cyst and post-haemorrhage calcification. (A-C) haemorrhagic hepatic cyst. Ultrasound (panel A) shows a cystic lesion surrounded by a thin wall. Presence of multiple septations that do not enhance on contrast-enhanced ultrasound (not shown). On MRI (T1- and T2-weighted MRI) the lesion is strongly hyperintense on T2 and has intermediate signal on T1. Internal septations are strongly hyperintense on T1 and correspond to haemorrhagic septations. (D) Calcification after cyst haemorrhage.

- **Conservative Mx** – Avoid interventions during active hemorrhage
- **Temporary interruption** of anticoagulants is recommended
- Anticoagulants – resumed 7–15 days after the onset of haemorrhage
- **Restart earlier** – if high risk for thromboembolism
- **No role for the administration:**
  - vitamin K, PCC or FFP - unless haemodynamic instability
- **OMIT** aspirin for 3 days following the onset of cyst haemorrhage
- **DUAL antiplatelet Rx:**
  - Cont the clopidogrel, OMIT Aspirin for 3 days

Cyst infection

Table 3. Criteria for hepatic cyst infection and radiological findings suggestive of hepatic cyst infection.

Criteria definite hepatic cyst infection	Criteria likely hepatic cyst infection (after exclusion of other sources)
• Cyst aspiration showing evidence of infection (neutrophil debris and/or microorganism)	• Fever (temperature >38.5°C for >3 days) with no other source of fever detectable • CT or MRI detecting gas in a cyst • ^{18}FDG PET-CT showing increased FDG activity lining a cyst compared to normal parenchyma • Tenderness in the liver area • Increased C-reactive protein • Increased leukocyte count (>11,000/L) • Positive blood culture

Radiological findings suggestive of hepatic cyst infection
• Liver ultrasound: debris with a thick wall and/or a distal acoustic enhancement in at least one cyst • Liver CT/MRI: enhanced wall thickening and/or perilesional inflammation in at least one cyst • MRI: high signal intensity on diffusion-weighted images, fluid-fluid level, wall thickening, or gas in at least one cyst • Positron emission tomography scan (^{18}FDG PET-CT): increased FDG activity lining a cyst compared to normal parenchyma

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Management

- **Fluoroquinolones and 3rd-generation cephalosporins** – 4-6wks
- Carbapenems + Cefazolin= poor penetration
- **Approach:**
  - Use quick sequential organ failure assessment
  - Tailor antibiotic therapy to blood cultures
  - Adjust antibiotic therapy to the local resistance profile
  - Adapt drug dosage to renal function
  - Fungal infection if antibiotics do not lead to clinical improvement
- **Success:**
    - RESOLUTION of symptoms including fever
    - Normalisation of CRP
    - At least 2 negative blood cultures

Box 1. Factors for drainage of infected hepatic cysts.

- Persistence of temperature >38.5° C after 48 hours on empirical antibiotic therapy
- Isolation of pathogens unresponsive to antibiotic therapy from a cyst aspirate
- Severely compromised immune system
- CT or MRI detecting gas in a cyst
- Large infected hepatic cysts

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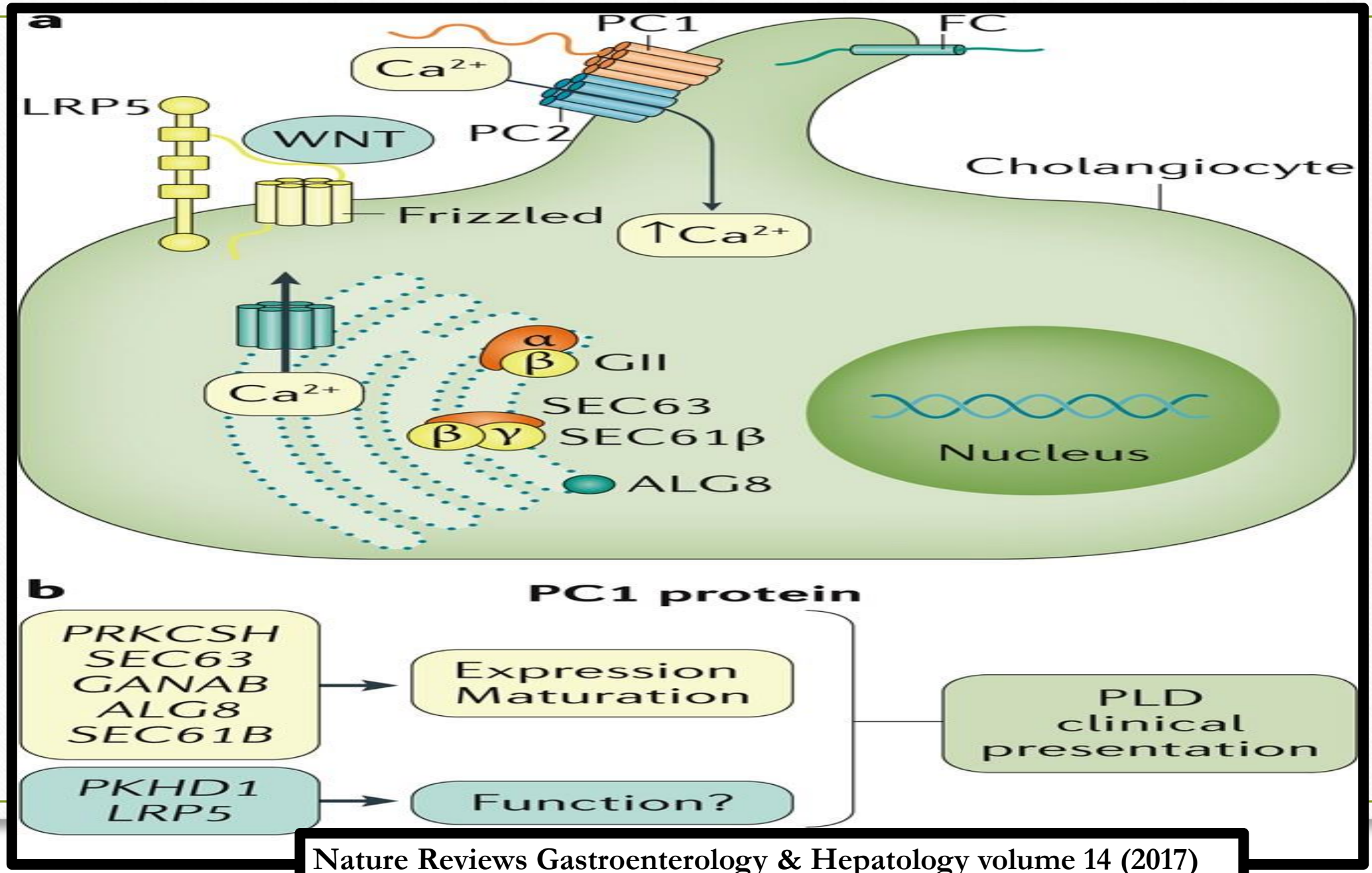
Polycystic liver disease

- **Rare –** 1/10 000- 1/158 000
- ≥ 10 hepatic parenchymal cysts unconnected to the bile duct system
- ADPKD/ADPLD
- Earlier onset and faster progression in females
- **2mm to ≥10 cm**
  - Single layer of cuboidal or columnar epithelium, resembling that of bile ducts
  - Rarely squamous epithelium – risk SCCa
- **ADPKD – 30yrs (24%) & 60yrs (80%) –** Renal disease predominates
  - Pancreatic/spleen, diverticular disease, inguinal hernias, MVP, Berry aneurysms
- **ADPLD-**2-5% symptomatic



Nature Reviews Gastroenterology & Hepatology volume 14 (2017)

	Associated disease	Renal phenotype	Extra-renal phenotype
Classical ADPKD*			
PKD1[3,20]	ADPKD-*PKD1* with truncating mutation	Innumerable bilateral kidney cysts causing progressive kidney enlargement and reduction in eGFR; median age at ESKD about 55 years	Polycystic liver disease, mild to severe
PKD1[3,20]	ADPKD-*PKD1* with non-truncating mutation	Innumerable bilateral kidney cysts causing progressive kidney enlargement and reduction in eGFR; median age at ESKD about 67 years	Polycystic liver disease, mild to severe
PKD2[3,20]	ADPKD-*PKD2*	Innumerable bilateral kidney cysts causing progressive kidney enlargement and reduction in eGFR; median age at ESKD about 79 years	Polycystic liver disease, mild to severe
ADPKD-like phenotype			
GANAB[14,15]	ADPKD-*GANAB*	Bilateral renal cysts, preserved kidney function	Polycystic liver disease, mild to severe
DNAJB11[18]	ADPKD-*DNAJB11*	Normal or small-sized kidneys with multiple small renal cysts; possible evolution to ESKD after 60 years	Polycystic liver disease, absent to moderate
ADTKD-associated genes			
HNF1B[21]	ADTKD-*HNF1B*	Bilateral renal cysts in about 45% c ADPKD imaging presentation; evo childhood-onset ESKD to preserve	
MUC1[22]	ADTKD-*MUC1*	Normal or small-sized kidneys, few to ESKD highly variable, age 20–70	
SEC61A1[16]	ADTKD-*SEC61A1*	Normal or small-sized kidneys, bila individuals	
UMOD[23]	ADTKD-*UMOD*	Normal or small-sized kidneys, few unilateral or bilateral; evolution to	
ADPLD-associated genes			
PRKCSH[24]	ADPLD	Few renal cysts occasionally reported	Polycystic liver disease, mild to severe
SEC63[24]	ADPLD	Few renal cysts occasionally reported	Polycystic liver disease, mild to severe
ALG8[34]	ADPLD	Few renal cysts occasionally reported	Polycystic liver disease, mild to moderate
SEC61B[34]	ADPLD	No renal cysts observed to date in the two families reported with a pathogenic mutation in this gene	Polycystic liver disease, mild to moderate
LRP5[25,26]	ADPLD	Few renal cysts occasionally reported	Polycystic liver disease, mild to moderate
Recessive inheritance			
PKHD1[27]	ARPKD	Antenatally enlarged hyperechogenic kidneys; multiple bilateral millimetre-sized cysts; ESKD in the first decade of life in about 50% of individuals but milder renal presentation with diagnosis in adulthood possible	Congenital hepatic fibrosis, Caroli syndrome, small liver cysts in heterozygous patients
DZIP1L[28]	ARPKD	Antenatal enlarged hyperechogenic kidneys; multiple bilateral millimetre-sized cysts; progression to ESKD variable (second and third decade of life)	No obvious extra-renal manifestations reported in the seven patients identified to date
PMM2[37]	Hyperinsulinaemic hypoglycaemia with PKD	Antenatal enlarged hyperechogenic kidneys, enlarged kidneys with multiple cysts; progression to ESKD variable, from infancy to early adulthood	Hyperinsulinaemic hypoglycaemia; small liver cysts in some patients
Syndromic forms of PKD			
TSC1 or *TSC2*[29,30]	Tuberous sclerosis	Multiple and bilateral angiomyolipomas and renal cysts; kidney function usually preserved; possible evolution to ESKD, either by destruction of the renal parenchyma by multiple angiomyolipomas or following nephrectomies for haemorrhagic angiomyolipomas; if there is contiguous gene deletion of *TSC2* and *PKD1*, severe PKD with evolution to ESKD occurs before age 30 years	CNS (cortical tubers, astrocytomas, epilepsy, and mental retardation); skin lesions (facial angiofibromas and hypopigmented spots); pulmonary lymphangioleiomyomatosis; cardiac rhabdomyoma and retinal hamartoma; polycystic liver disease if contiguous deletion of both *PKD1* and *TSC2*
VHL[31]	Von Hippel-Lindau disease	Bilateral renal cysts, renal cell carcinoma	Haemangioblastomas of the retina, spine, or brain; pheochromocytoma; neuroendocrine tumour of the pancreas
COL4A1[32,33]	HANAC syndrome or *COL4A1*-related disease	Bilateral renal cysts occasionally reported; patients can develop renal insufficiency after about age 50–60 years	Microscopic haematuria, aneurysms, muscle cramps, elevated creatine phosphokinase, tortuosity of the retinal arteries
OFD1[34,35]	Oro-facial-digital syndrome type 1	X-linked, embryonically lethal in boys, PKD in women	Cleft palate, facial dysmorphy; syndactyly, clinodactyly, or polydactyly; mental retardation; polycystic liver disease

Cornec-Le Gall et al, Lancet 2019

Clinical Features

- **Usually asymptomatic**
- **Symptoms** – female/larger & more numerous cysts (10-15%)
  - Abdominal pain/discomfort, postprandial fullness, hepatomegaly, dyspnoea
- **Severe pain**:
  - Infection, intracystic hemorrhage, rupture, pendunculated cyst torsion, jaundice (5%)
  - Ascites/Hepatic hydrothorax – PHT (congenital hepatic fibrosis) – rarely varices

Polycystic liver disease-related symptoms	Polycystic liver disease-related complications
Abdominal fullness	Jaundice
Lack of appetite or early satiety	Hepatic venous outflow obstruction
Acid reflux	Portal hypertension
Nausea and vomiting	Recurrent cyst infection
Pain in rib cage, sides, abdomen or back	Recurrent cyst haemorrhage
Shortness of breath	
Limited mobility	
Fatigue	
Anxiety about the future	
Concern or dissatisfaction with abdomen size	
Problems with intercourse	
Involuntary weight loss	

Diagnosis

- **LFTs** normal- Mildly elevated ALP/GGT
- **CA19.9** – elevated
- **Confirmed**– U/S; CT & MRI
- **KDIGO** – AUS for all ADPKD
- No need to screen family members of PLD unless symptoms develop
- Liver volume - **1.8% annually** (4.8% females 40YRS) **– prognostic marker**
  - Pts counselled on the growth pattern – symptoms arise (expert centres)
  - No need to screen family
- Little room for genetic testing

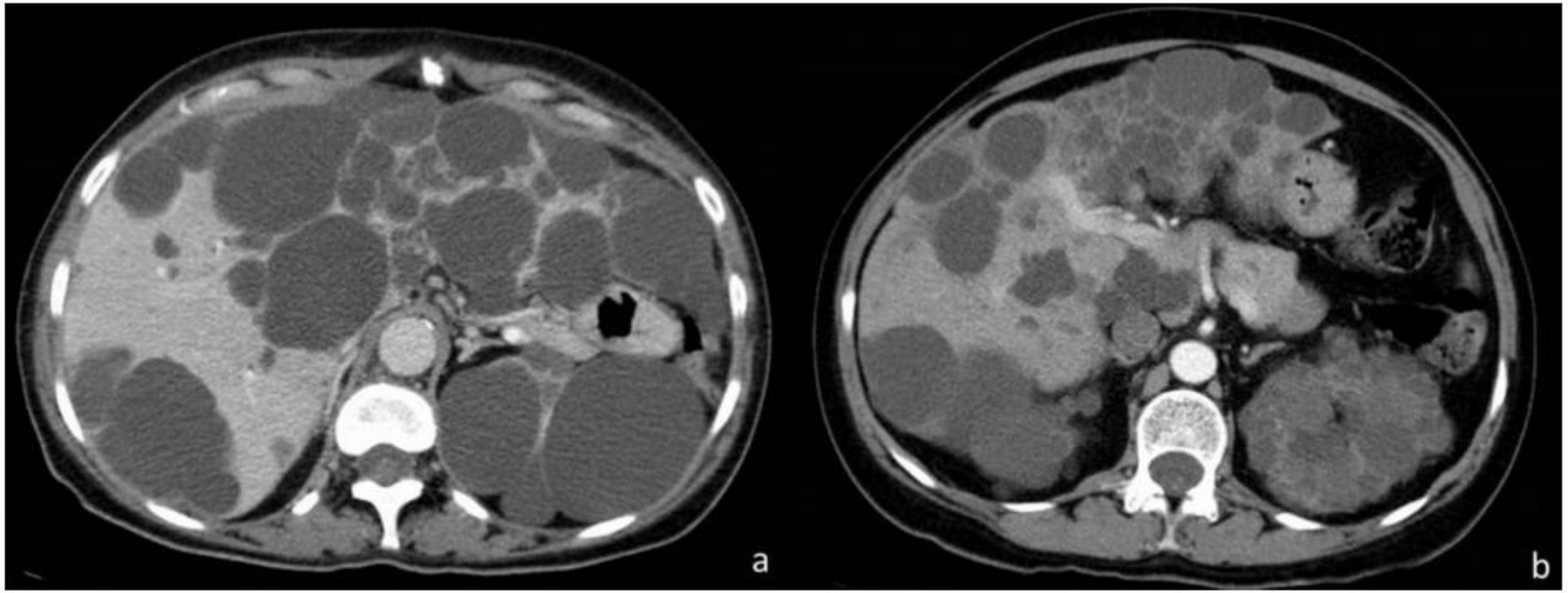
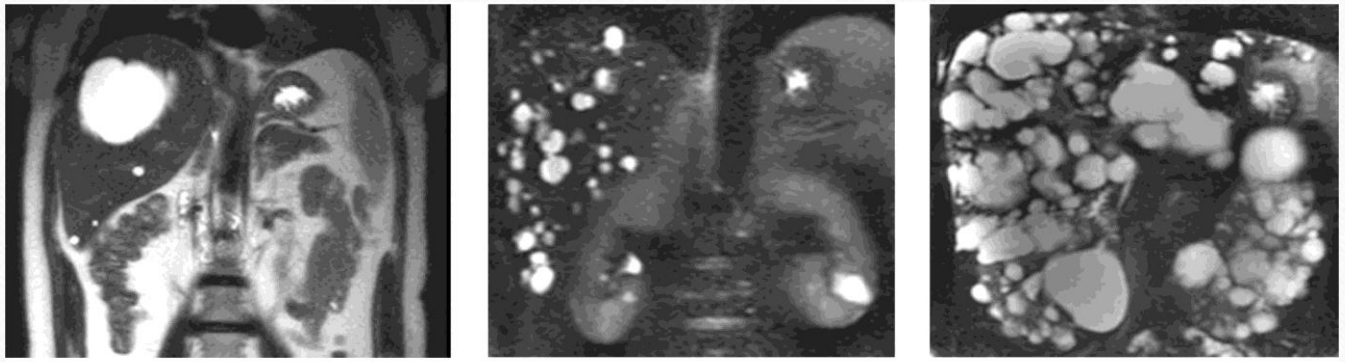


Fig. 3: Contrast enhanced abdominal CT of a patient with polycystic liver disease, showing multiple simple cystic lesions in the liver and kidneys. Image b shows numerous cysts in the left lobe of the liver, some of them with polygonal borders.

Gigot Criteria

- Type 1: <10 large hepatic cysts, >10cm
- Type 2: Diffuse involvement of liver parenchyma by multiple medium sized cysts with remaining large areas of patent liver parenchyma
- Type III: Diffuse involvement of liver parenchyma by different sized liver cysts with slight areas of normal liver parenchyma



Clinical Liver Disease 2019

Qian's Classification

- used mainly for family member screening
- Grade 0: no cyst
- Grade 1: 1-10 cysts
- Grade 2: 11-20 cysts
- Grade 3: >20 cysts
- Grade 4: >20 cysts and symptomatic hepatomegaly

Schnelldorfer

	Type			
	A	B	C	D
Symptoms	Absent or mild	Moderate or severe	Severe	Severe
Cyst findings	Focal	Focal	Diffuse	Diffuse
Normal hepatic segments	≥3	≥2	≥1	<1
Portal vein/hepatic vein occlusion	No	No	No	Yes

Stop exposure to exogenous oestrogens

Polycystic liver disease

No cyst-related symptoms

No treatment or follow-up

Cyst-related symptoms

Numerous small to medium sized cysts throughout the liver

Somatostatin analogues

Large or strategically located cyst percutaneously accessible

Aspiration sclerotherapy

Single or multiple large superficial cysts

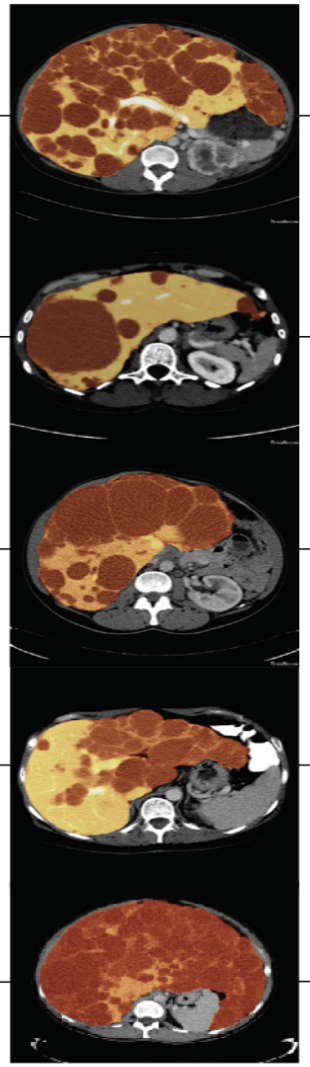
Cyst fenestration

Small to medium sized cysts clustered in a few segments in the presence of some less affected liver segments

Resection

Massive polycystic liver disease, severely affecting quality of life or accompanied by recurrent complications

Transplantation



Use symptom severity questionnaires to assess polycystic liver disease related symptoms and efficacy of treatment

Further Management

- **Stop exogenous estrogen** – levonorgestrel IUD, pregnancy is not C/I
- **Cyst rupture/haemorrhage/infection**
- **Hepatic vein obstruction-** Hepatic vein stenting
  - 78% - moderate , 22% - severe
- **Mitral valve prolapse –** Cardiologist
- **Family history of Berry aneurysms**– Screen. **No family history** – Counsel on risks

Further Management

- **Malnutrition** (Compression of stomach). Weight loss often underestimated

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  - Somatostatin analogues (Lanreotide, Octreotide) – decrease liver volume and increase intake. No effect on nutrition. Biggest reduction in first 6 months. Young women with rapidly progressive disease benefit most.
  - **AEs: Steatorrhoea, cholelithiasis, hypo- and hyperglycaemia and alopecia**
  - CT for Sarcopenia- Intensive nutritional optimization and exercise
  - Indications for LT

Criteria to refer patients with polycystic liver disease for liver transplantation

1. Clinically apparent liver disease due to massive polycystic liver severely affecting quality of life
2. Massive polycystic liver disease and complication(s), that can exclusively be treated by liver transplantation

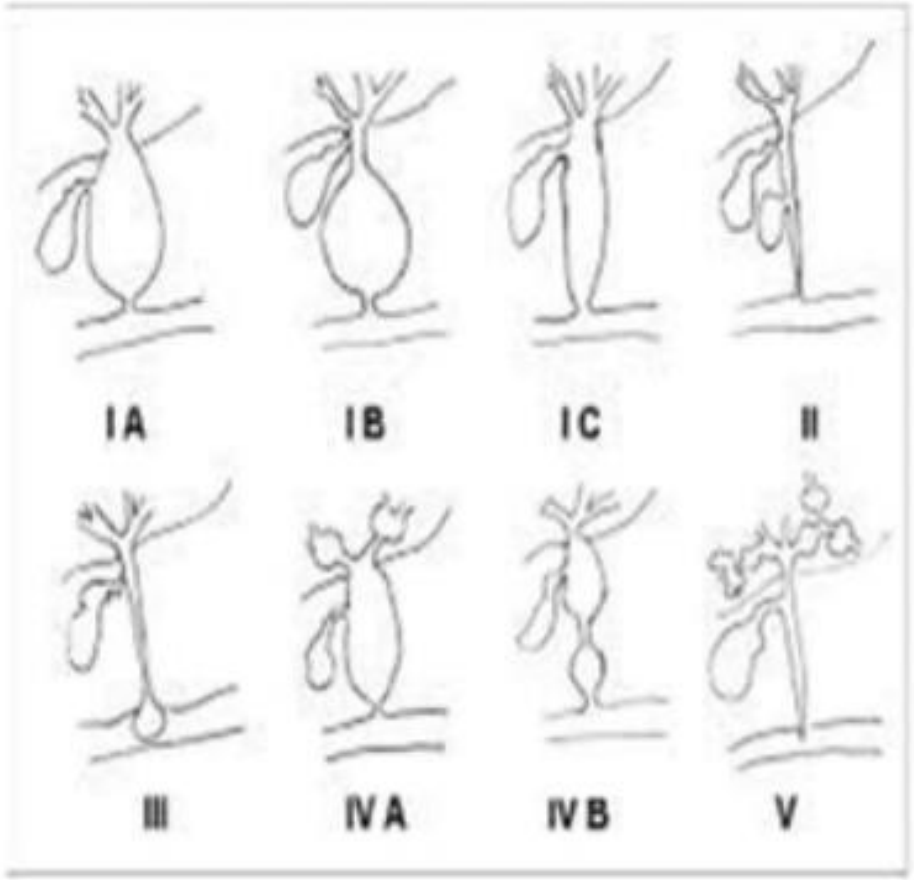
Complications include: severe malnutrition, hepatic venous outflow obstruction, ascites, portal hypertension, variceal haemorrhage, recurrent hepatic cyst infections

3. Failure of non-transplant related interventions and contraindications for non-transplant related interventions

Criteria to consider referral for combined liver-kidney transplantation

1. Creatinine clearance <30 ml/min

Todani Classification



Type-IA	cystic dilation of the extrahepatic duct.
Type-IB	Focal segmental dilation of the extrahepatic duct
Type-IC	Fusiform dilation of the entire extrahepatic bile duct.
Type-II	simple diverticula of the common bile duct.
Type-III	cyst/choledochocele distal intramural dilation of the common bile duct within the duodenal wall.
Type-IVA	combined intrahepatic and extrahepatic duct dilation
Type-IVB	multiple extrahepatic bile duct dilations.
Type-V	Caroli disease/ multiple intrahepatic bile duct dilation

Caroli Disease + Syndrome

- Ductal plate malformation of the large intrahepatic bile ducts.
- Failure of proper remodelling and resorption of the ductal plate during foetal development → persistence of embryonic biliary structures.
- Likely on phenotypical spectrum of ARPKD (PKHD1 mutations)
- Caroli Disease: Multifocal segmental dilatation of the large intrahepatic ducts
- Caroli Syndrome: Above + small intrahepatic ducts + congenital hepatic fibrosis
- Prevalence of cholangiocarcinoma =7%
- carcinogenic effects of chronic inflammation due to recurrent cholangitis, carcinogenic effects of biliary stasis, or formation of carcinogens due to permanent biliary irritation caused by gallstones.

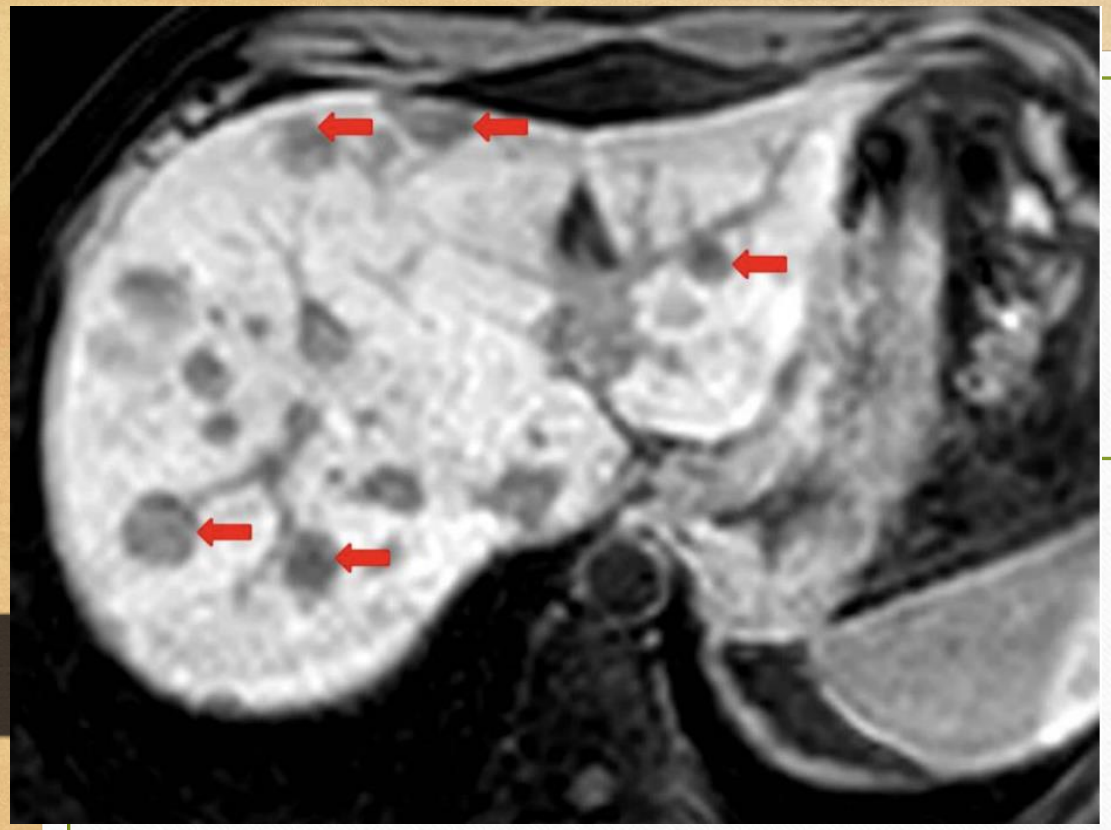


Fig. 5: Axial unenhanced T1-weighted MR image of a patient with Caroli disease, showing multiple hypointense cystic structures (arrows), corresponding to saccular dilatations of the biliary tree.

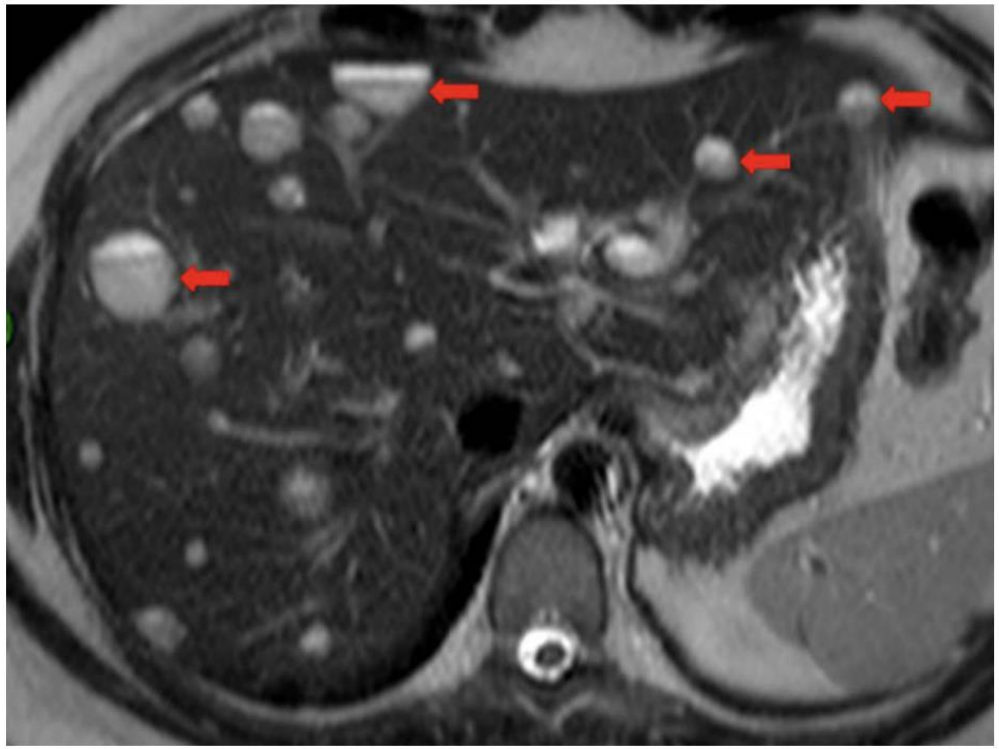


Fig. 6: Axial T2-weighted MR image showing multiple hyperintense cystic lesions (arrows), corresponding to intrahepatic bile duct dilatations in a patient with Caroli disease.

Clinical presentation

- Cholestasis--> stone formation, cholangitis, abscess formation
- Liver fibrosis (can be assessed by non-invasive methods)
- Portal hypertension
- Cholangiocarcinoma
- Renal: fusiform dilatations of renal collecting ducts and distal tubuli-> renal impairment

Management

- Cholangitis: antibiotics/ERCP
- Gallstones: UDCA(13-15 mg/kg/day)
- Abscesses: drainage
- Monitor for complications(osteoporosis)
- Surveillance for cholangiocarcinoma- yearly MRCP after dx
- ERCP not recommended for cholangio screening (risk of biliary infection)

Surgical Management

- **Liver resection:** Relieves symptoms, particularly in patients with Caroli disease with restricted bile duct involvement
- **Liver transplant:** If Recurrent cholangitis and 1). Bi-lobar involvement or 2). Mono-lobar involvement in combo with liver fibrosis or portal hypertension and liver resection not an option
- *Cholangiocarcinoma:* contra-indication for liver transplantation, though a study in patients with cirrhosis suggests that liver transplantation may be performed for cholangiocarcinoma of <−2 cm. Up to 75% recurrence rate

Biliary hamartomas

- also referred to as Von Meyenburg complexes are considered part of the spectrum of the ductal plate abnormalities
- They may occur in an otherwise normal liver or in association with Caroli disease, congenital hepatic fibrosis, and ADPKD or ADPLD.
- Tiny (<1cm) hypodense lesions throughout liver with normal intra and extrahepatic ducts
- Typically 2-10mm
- "starry-sky appearance"= irregular shapes with well defined margins
- If asymptomatic, no need to follow up

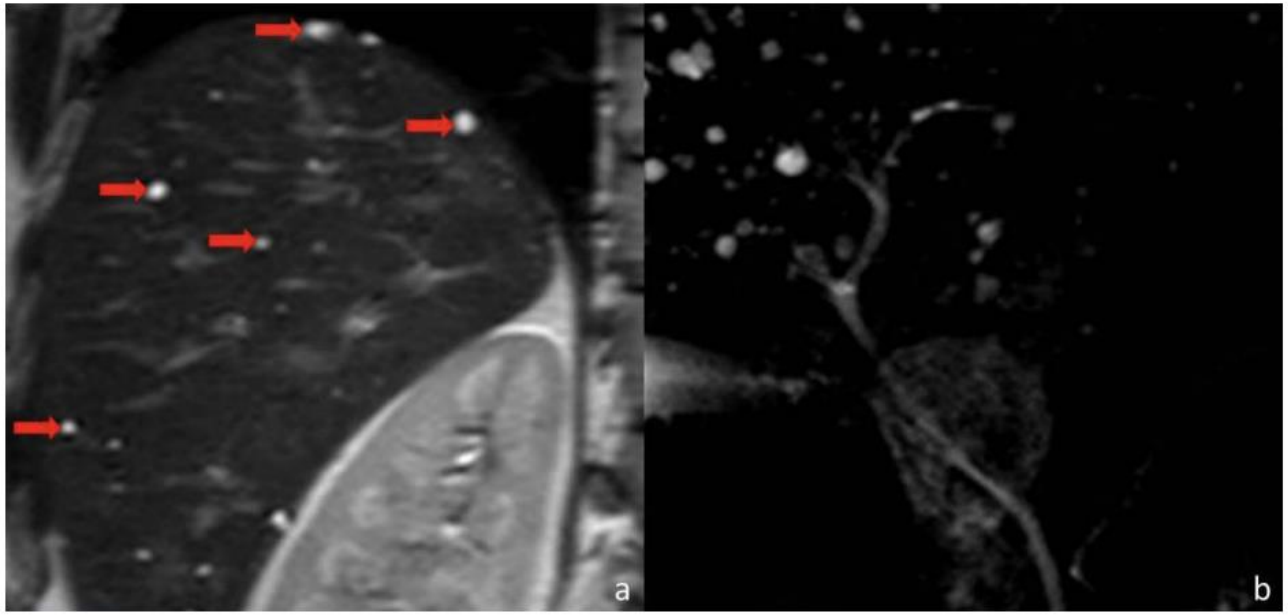
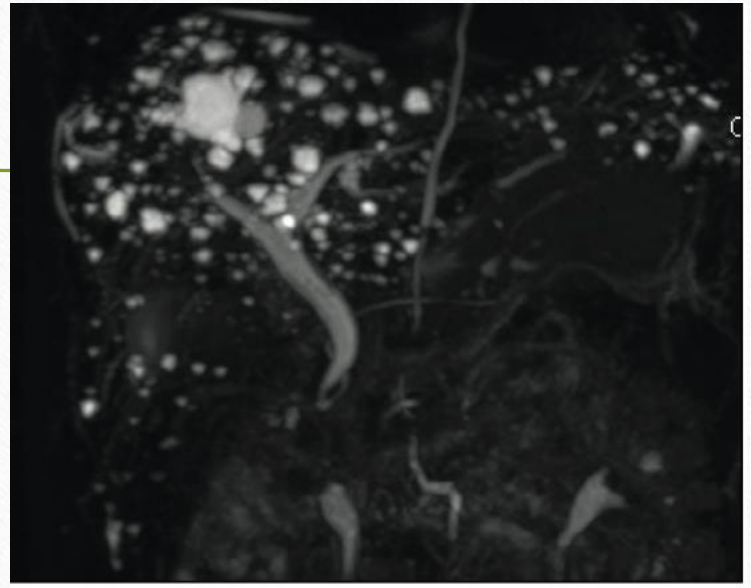


Fig. 4: (a) Coronal T2-weighted MR image; (b) MRCP coronal projection, showing bile duct hamartomas in the liver of a young healthy woman.



MRI: Imaging of choice

Mucinous Cystic Neoplasms

- <1% of liver cysts
- Females
- 5^{th}-6^{th} decade

- Most centrally located but can be found in right or left lobe
- Cystic epithelial neoplasm lined by cuboidal, columnar or flattened mucin-producing epithelium overlying ovarian-like hypercellular stroma
- Size varies from 1.2 cm to 40cm, mean 15cm
- Vast majority benign (3-6% invasive carcinoma)

Table 1: Comparison World Health Classification of Mucinous Cystic Liver Neoplasms

WHO 2000 Prior Nomenclature	WHO 2010 Current Nomenclature	Key Features
Biliary cystadenoma	Non-invasive Biliary Mucinous Cystic Neoplasm (ni-BMCN)	Needs ovarian-like stroma No typical bile duct communication
Biliary cystadenocarcinoma	Invasive Biliary Mucinous Cystic Neoplasm (i-BMCN)	Needs ovarian-like stroma No typical bile duct communication
Not previously classified	Intraductal papillary mucinous neoplasm – biliary type (IPMN-B)	No ovarian-like stroma Needs bile duct communication

Kloppers et al, South African Gastroenterology Review, 2016

Histology

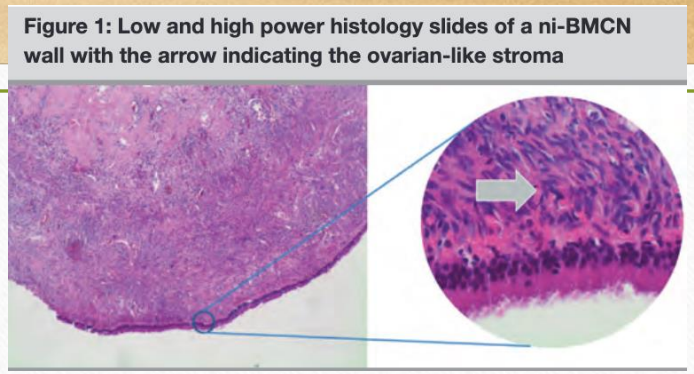
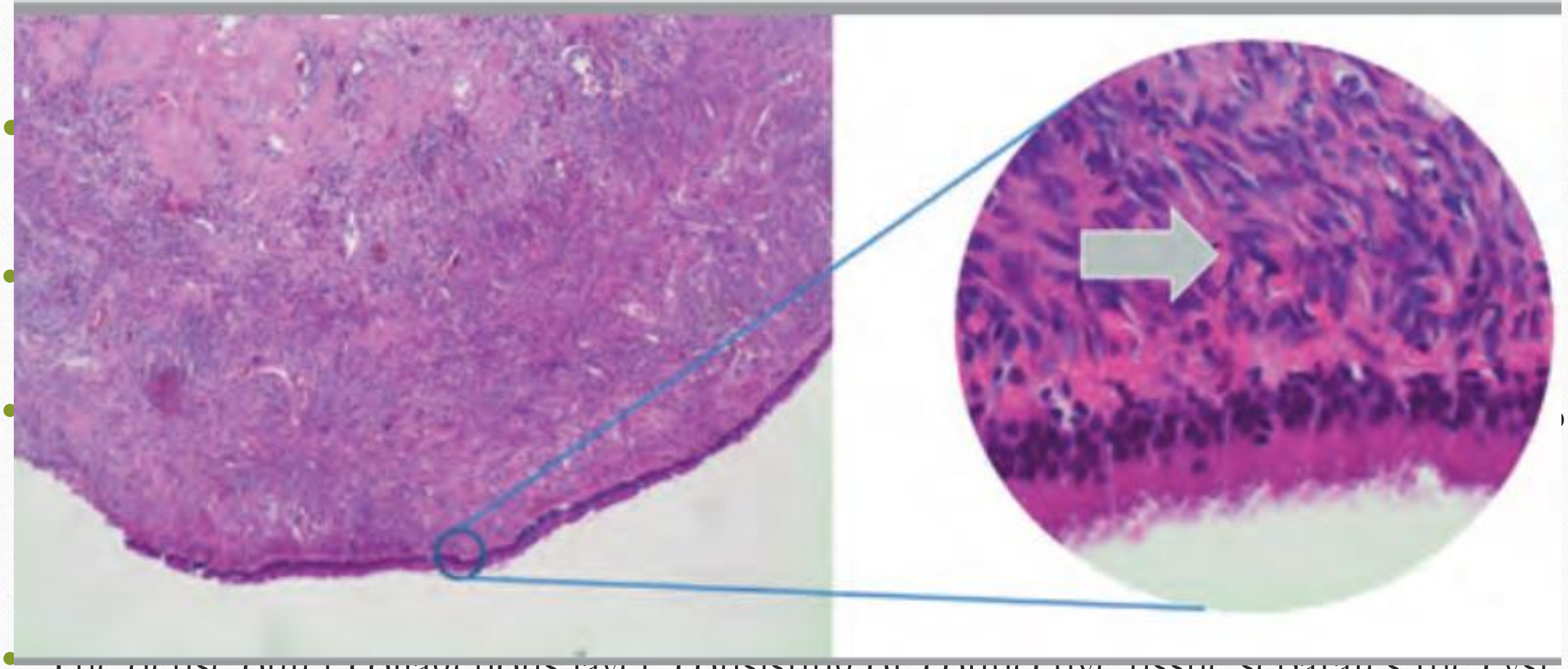


Figure 1: Low and high power histology slides of a ni-BMCN wall with the arrow indicating the ovarian-like stroma

- cyst-forming epithelial neoplasm, usually with no communication with the bile ducts
- An inner biliary-type epithelial layer containing cuboidal to columnar cells which produce mucin.
- A layer of dense undifferentiated mesenchymal cells resembling ovarian stroma deep to the epithelial lining (Subepithelial).
  - The stromal cells are spindle-shaped and usually immunoreactive with vimentin, alpha-smooth muscle actin and less frequently estrogen and progesterone receptors.
- The dense outer collagenous layer, consisting of connective tissue separates the cyst from liver parenchyma- often provides a surgical plane for enucleation.

Figure 1: Low and high power histology slides of a ni-BMCN wall with the arrow indicating the ovarian-like stroma



- The dense outer collagenous layer, consisting of connective tissue separates the cyst from liver parenchyma- often provides a surgical plane for enucleation.

Clinical Presentation

- Commonly symptomatic (86%)
  - Abdominal pain
  - Fullness
  - Early satiety (mass effect)
- Low grade dysplasia, high grade dysplasia or invasive carcinoma

Table 4. Worrisome features in mucinous cystic neoplasms of the liver.

Major worrisome features	Minor worrisome features
Thick septation	Upstream biliary dilatation
Nodularity	Thin septations
	Internal haemorrhage
	Perfusional change
	<3 coexistent hepatic cysts

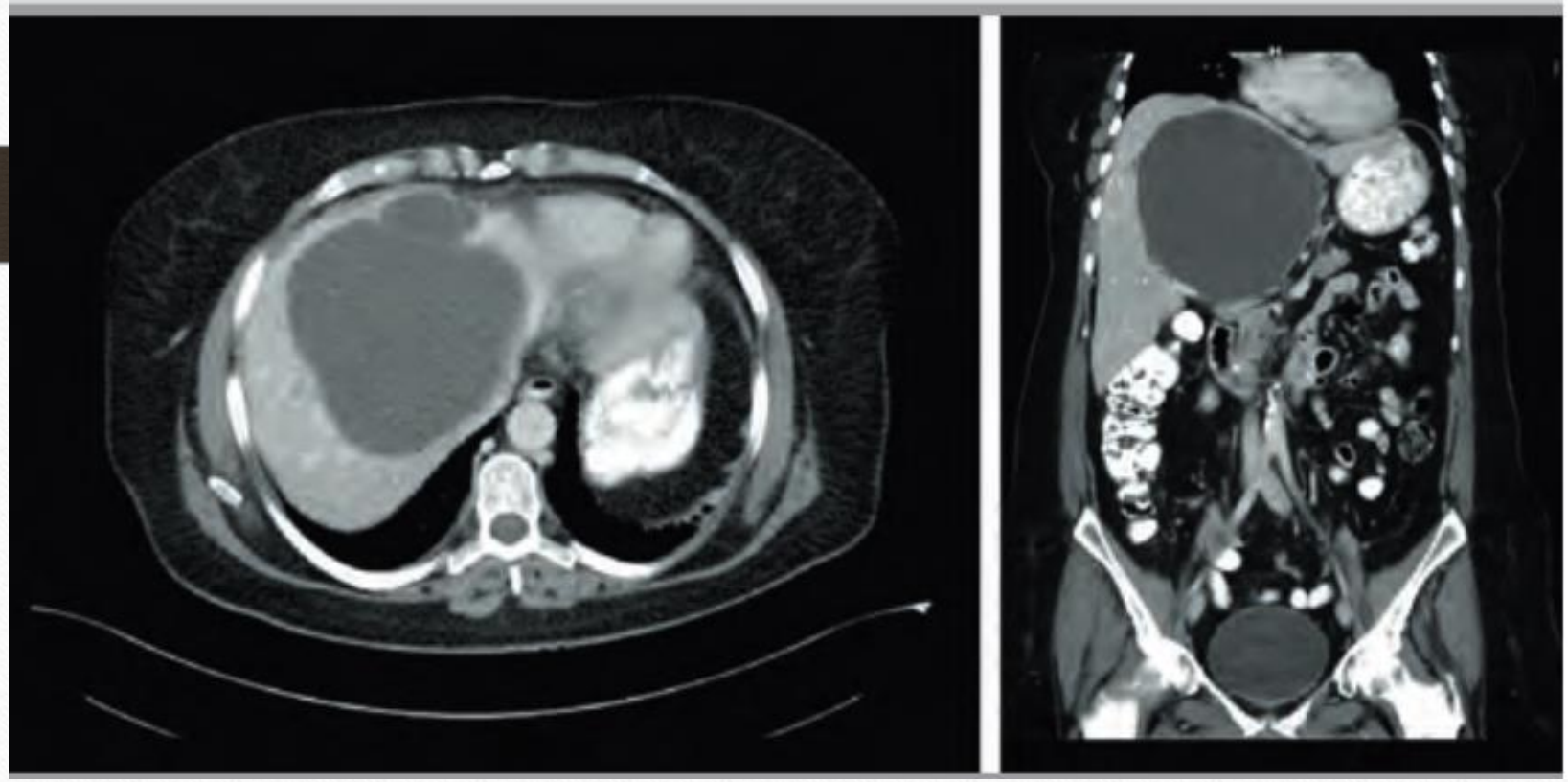
A combination of >−1 major and >−1 minor feature may be considered as worrisome features for MCNs of the liver.

MRI should be used to characterise hepatic cysts with worrisome features

TAG72) – Simple vs MCN (>25U/ml (Sen:79% & Spec:97%)

Investigations

Figure 2: CT Scan of a large centrally placed BMCN involving both R and L liver lobes



Typically solitary, large, well- circumscribed cystic lesions, either multiloculated (90%) or unilocular, mainly in LLL. Often contain enhancing septa, mural calcifications, and mural nodules, the latter being associated with malignancy if larger than 1 cm

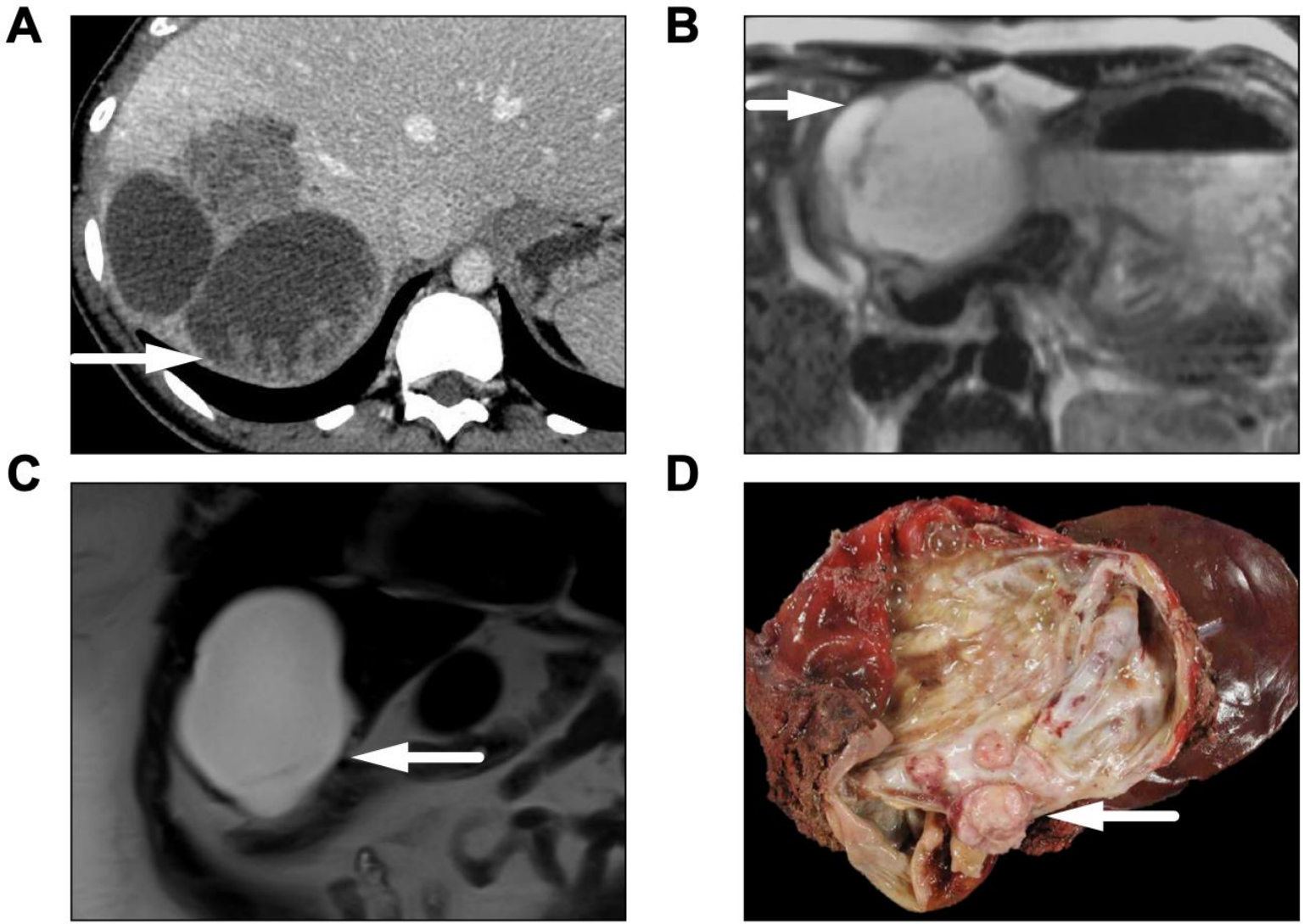
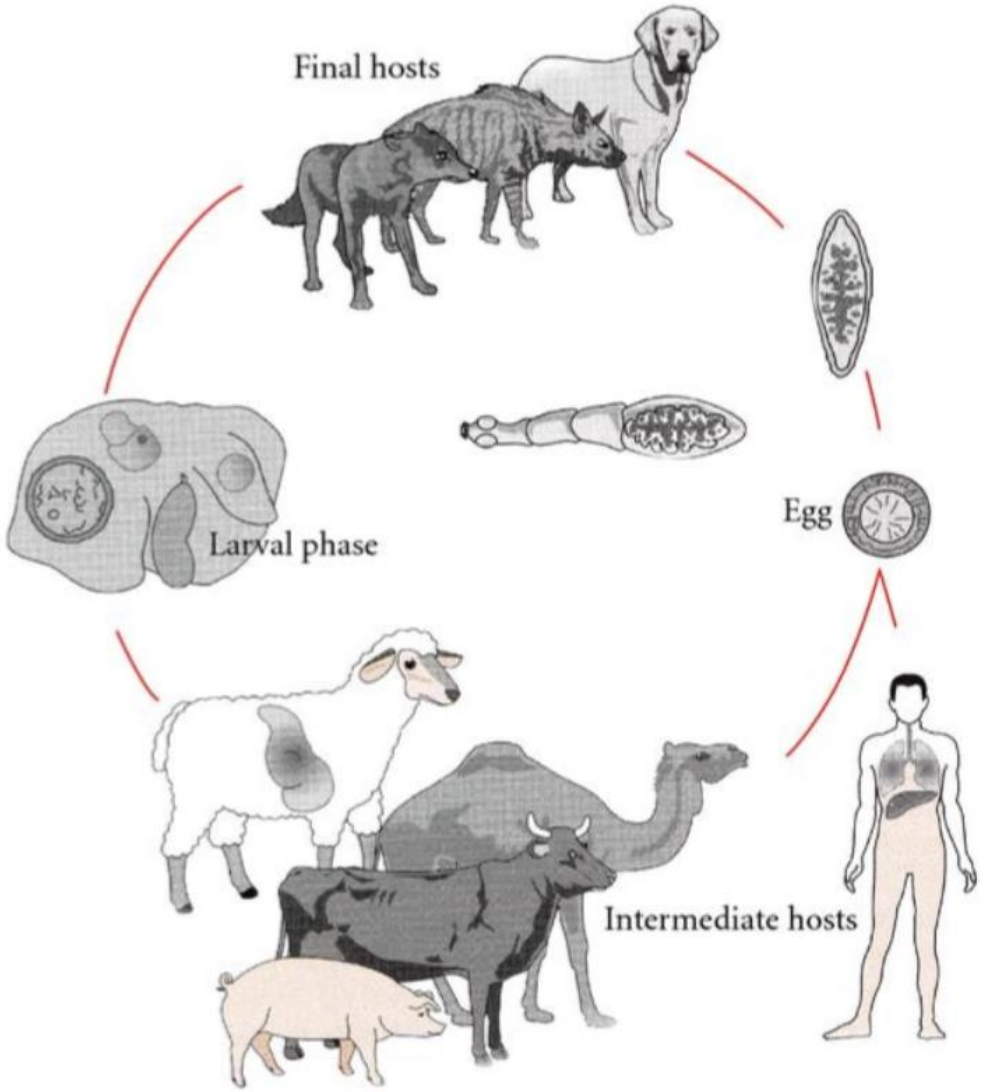


Fig. 3. Worrisome features in mucinous cystic neoplasms of the liver. (A) Malignant mucinous cystic tumour. Contrast-enhanced CT during the portal venous phase showing multiseptated cystic lesion of the right liver with multiple nodularity. (B,D) malignant mucinous cystic tumour. T2-weighted MRI sequence showing cystic lesion of the left liver with thick septations. Pathologic examination shows thick septations and internal nodularity. (C) Low-grade mucinous cystic tumour. Coronal T2-weighted MR sequence showing cystic lesion of the right liver with a thin septation at the lower part of the lesion.

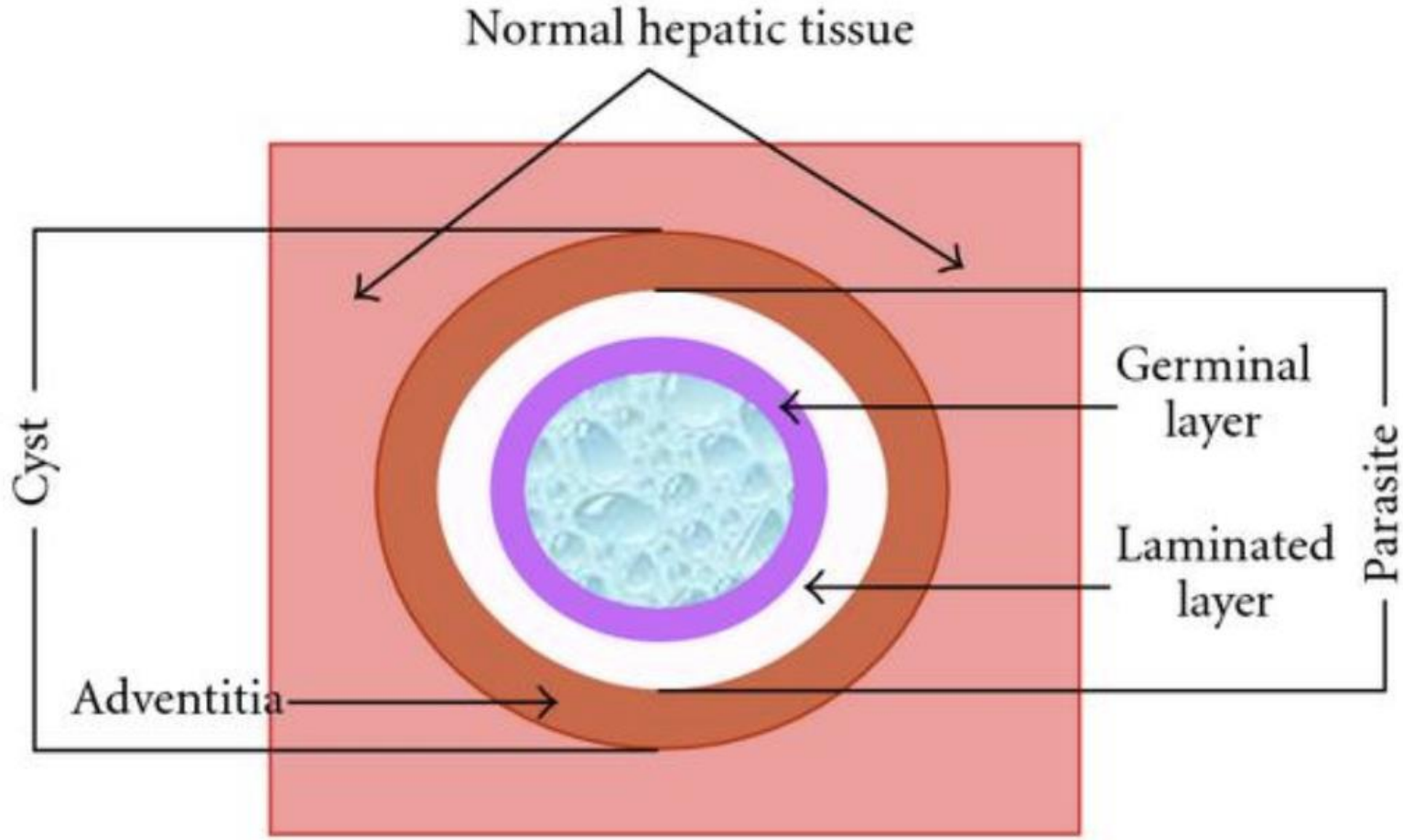
Management

- Mainstay→ Complete resection with negative margins (peripheral or one liver lobe)
- Enucleation if central and involving major vascular or biliary structures
- Aspiration, internal drainage, intra-tumoral sclerosant injection, incomplete resection→ 90-100% recurrence rate
- Irresectable disease: Fenestration and complete fulgaration of internal cystic lining

Hydatid Cysts



Echinococcus granulosus


Normal hepatic tissue
Cyst
Germinal layer
Laminated layer
Parasite
Adventitia

- Protoscolex is produced asexually within cysts in inner layer
- Rupture of the hydatid cyst→ releases these→ daughter cysts in secondary sites
- adult Echinococcus tapeworm consists of a scolex, which contains a rostellum with 20 to 50 hooklets and 4 suckers, a neck, and an immature, mature, and gravid proglottid.

Clinical presentation

- Initially asymptomatic

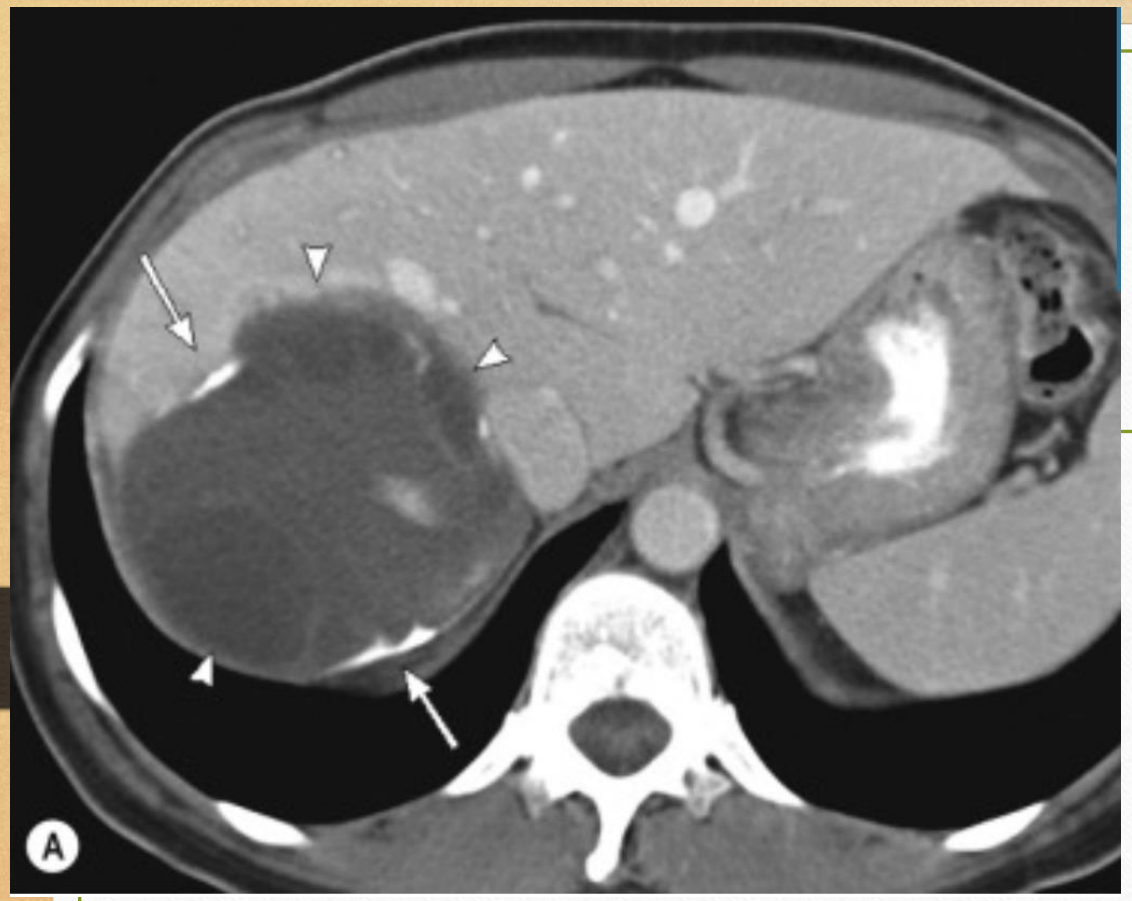
- Depends on type, size and site of cysts
- Grows 1-5cm per year
- Small ones can go undetected
- Large ones→ signs of compression or rupture
  - Biliary colic, cholangitis, obstructive jaundice, portal and venous obstruction, Budd-Chiari syndrome, bronchial fistula
  - Peritonitis/Anaphylaxis

Investigations

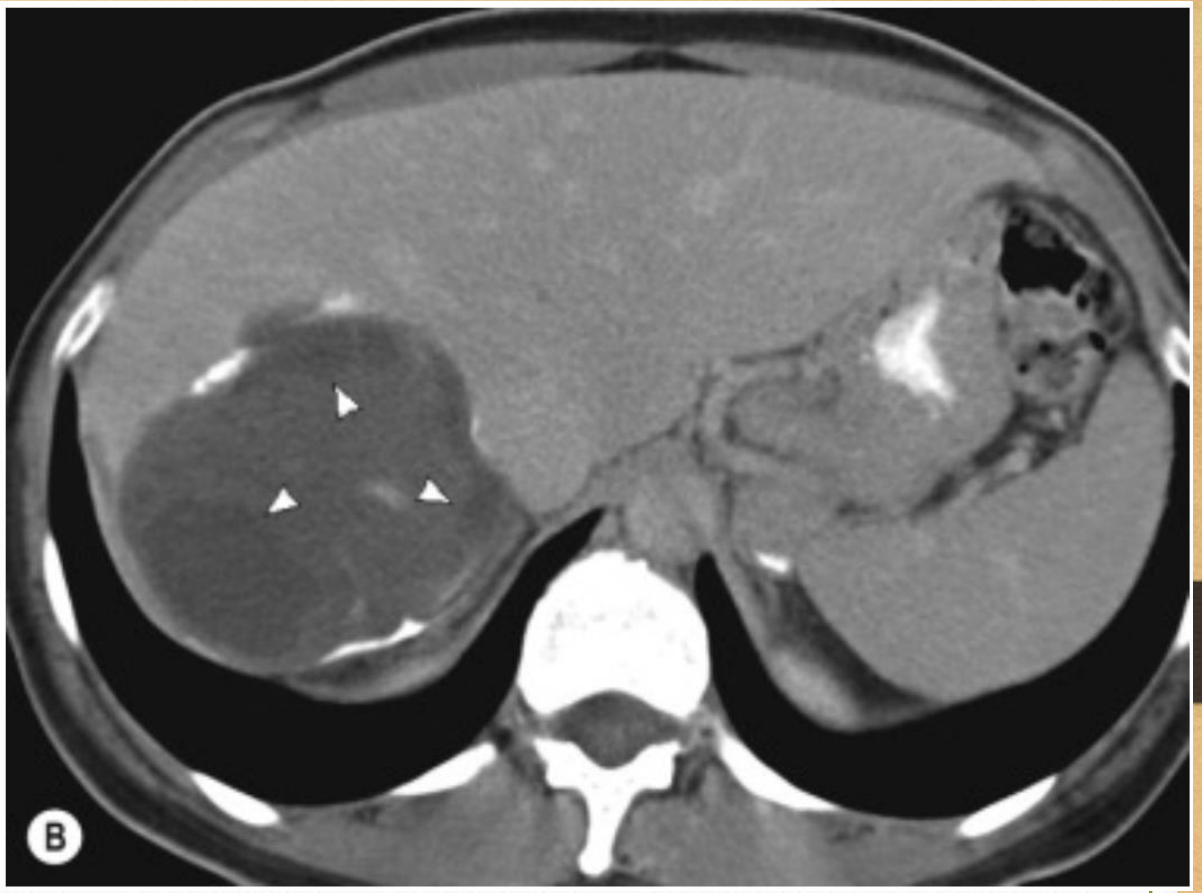
- Labs: FBC +diff, LFTS (elevated in ½ of cases), ALP (elevated in 90%), CRP and blood cultures (bacteraemia)
- Echinococcus serology-> + in liver and bone, - in rest(also if calcified)

Investigations

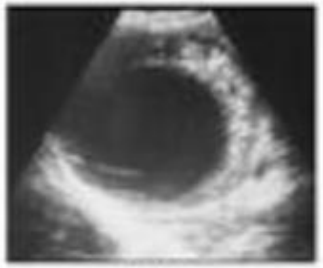
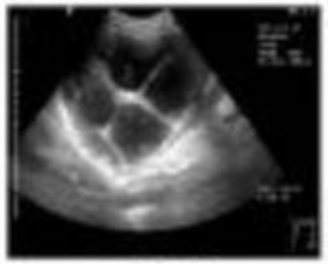
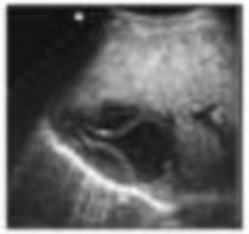
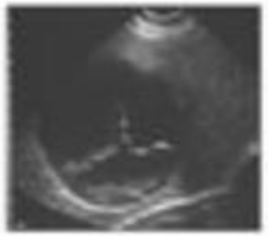
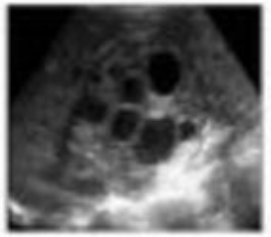
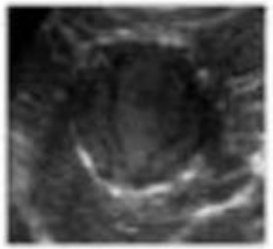
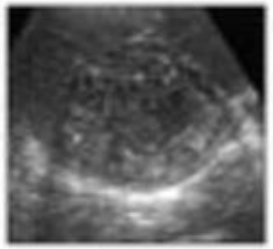
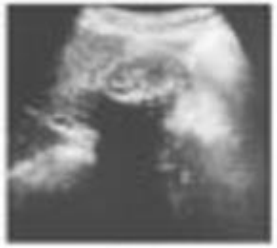
- AUS: test of choice
  - Complex cyst features: dependent debris, daughter cysts, membrane separation and wall calcification
- CT helpful and defines features esp if wall calcified
- MRI can define but insensitive to calcification



Axial portal venous phase CT: Large cyst with peripheral calcification and daughter cysts



Late phase CT demonstrates the absence of enhancement of the wall and internal septations (part of parasite). NB to differentiate from neoplasms and MCNs/Cystic mets

Gharbi 1981	WHO classification (cyst types)		
Type I	Univesicular anechoic cystic lesion with double line sign (CE1)	Active	 CE 1  CE 2
Type III	Multiseptated, "rosette-like"/ "honeycomb" cyst (CE2)		
Type II	Cyst with detached membranes "water-lilly-sign" (CE3a) Cyst with daughter vesicles in solid matrix (CE3b)	Transition	  CE 3a  CE 3b
Type IV	Cyst with heterogenous content (hypoechoic/hyperechoic). No daughter vesicles (CE4)	Inactive	  CE 4  CE 5
Type V	= CE4 plus calcified wall (CE5)		

Management

- Asymptomatic, inactive, calcified cysts: Manage expectatntly
- Chemotherapy alone only if patient not a candidate for primary percutaneous or surgical treatment, multiorgan dissemination or declines other intervention
- >40% of hydatid cysts remain active or reactivate after 2 years of monotherapy
- Recommend start before a procedure and 1-6/12 after

Percutaneous

- PAIR (Puncture, Aspiration, Injection and Reaspiration)
- Cysts >5cm who aren't surgical candidates or decline surgery, or relapse post-op.
- Not recommended if biliary fistulas present or communications with the biliary tree (biliary sclerosis)
- CI: inaccessible cysts, complicated multivesiculated cysts

Surgical

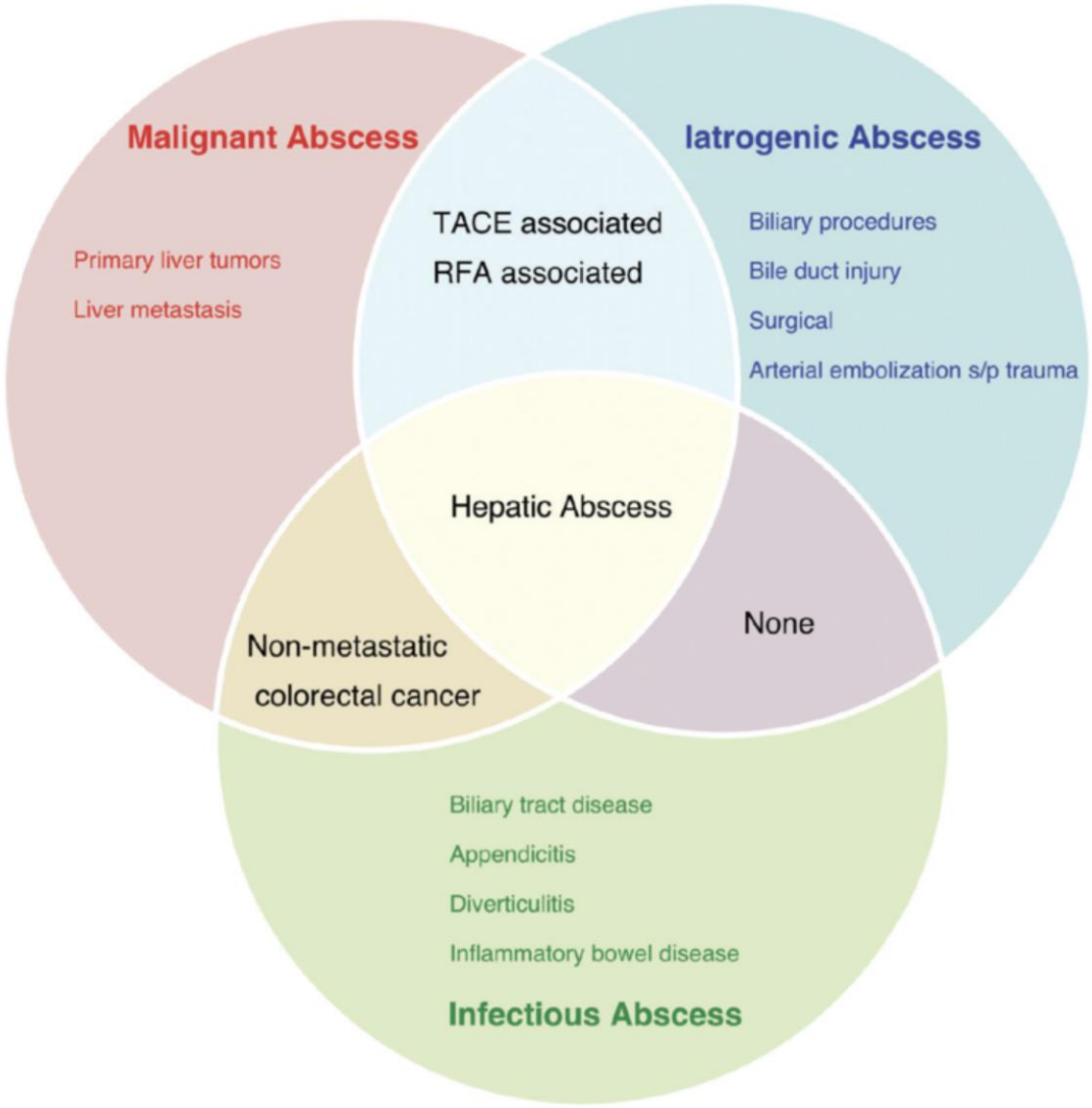
- Radical pericystectomy or conservative deroofing (complicated cysts that have fistulas, multiple daughter vesicles, rupture, haemorrhage or secondary infection).
- Hepatic resection (segmental/lobar)

Liver abscess

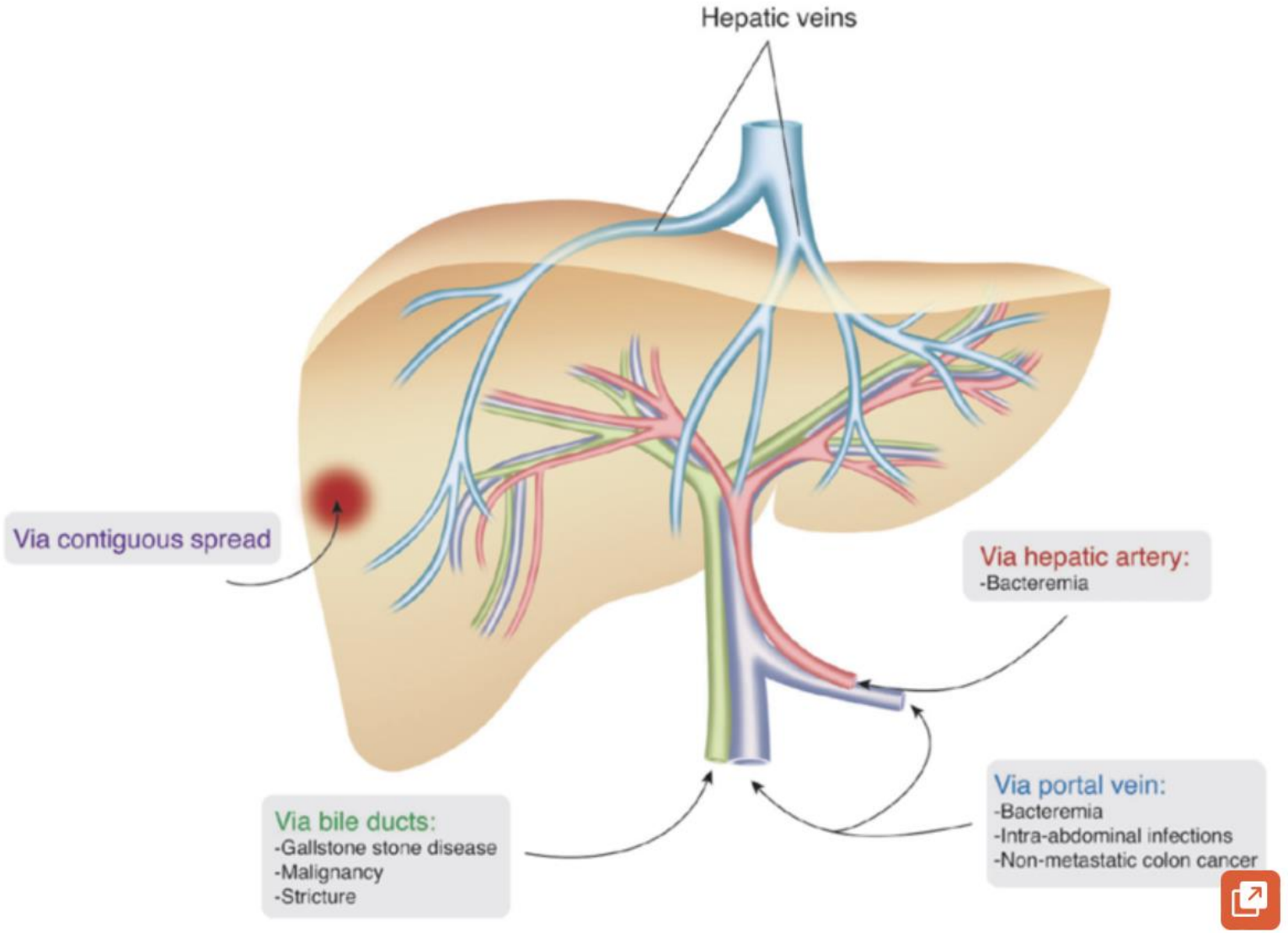
- Encapsulated collection of suppurative material within the liver parenchyma
- Low incidence 2.3/100 000 admissions (USA) 275/100 000 (Taiwan)

- Males>females
- Infectious
  - Pyogenic (80%)
  - Amoebic (10%)
  - Fungal (10%)
- Malignant
- Iatrogenic

Figure 1 - Categorization of hepatic abscesses



Taken from: Mavilia M, Molina M, Wu G. The Evolving Nature of Hepatic Abscess: A Review. J



Taken from: Mavilia M, Molina M, Wu G. The Evolving Nature of Hepatic Abscess: A Review. J Clin Transl Hepatol. 2016

Table 1 Etiology and mechanism related to liver abscess

Etiological organisms				Mechanism related
Gram negative aerobes	Gram-positive aerobes	Anaerobes	Miscellaneous	Portal pyemia
Klebsiella pneumoniae	*Enterococcus* sp.	*Bacteroides* sp.	*Actinomyces*	Ascending cholangitis
E. coli	*Staphylococcus aureus*	*Fusobacterium*	Tubercular	Malignant abscess
Pseudomonas sp.	*Streptococcus* sp.		*Candida albicans*	Iatrogenic (TACE, RFA)
Proteus sp.				Diverticulitis

Wadhera et al, J Gastrointest Infect 2022

Risk factors

- Increasing age
- Male sex
- Underlying DM
- Liver cirrhosis (15.4x higher risk)
- Continuous use of PPIs
- Immunocompromised state

} 2/3rd of all patients=males in 4th-5th decade

Signs and symptoms

- Fever/malaise/abdominal pain= 1/3rd of cases

- Jaundice, loss of weight in 1/4
- Nausea/vomiting
- 10% diarrheal illness
- Abdo pain→ RUQ. Inflamm of liver capsule (subcapsular abscess) or stretch of capsule (hepatomegaly) or GB wall oedema
- Less frequent: right pleural effusion, jaundice, ascites, Murphy's sign, hypotension

Investigations

Bloods:

- Raised WCC.
- 50% have raised ALT/bili
- 85% raised ALP
- Abnormal INR in 13%

All non-specific

- AUS: sensitivity 85%
- well-defined round lesion with central hypoattenuation → enhancement of the rim and internal septa due to increased vascularity in these parts.
- Heterogeneous with poorly marginated borders and irregular contours (pre-suppurative) → a delineated hypodense lesion with a thick capsule during the suppurative phase.
- The presence of air is a pathognomonic sign, though it is present only in 15 to 20% of the cases.

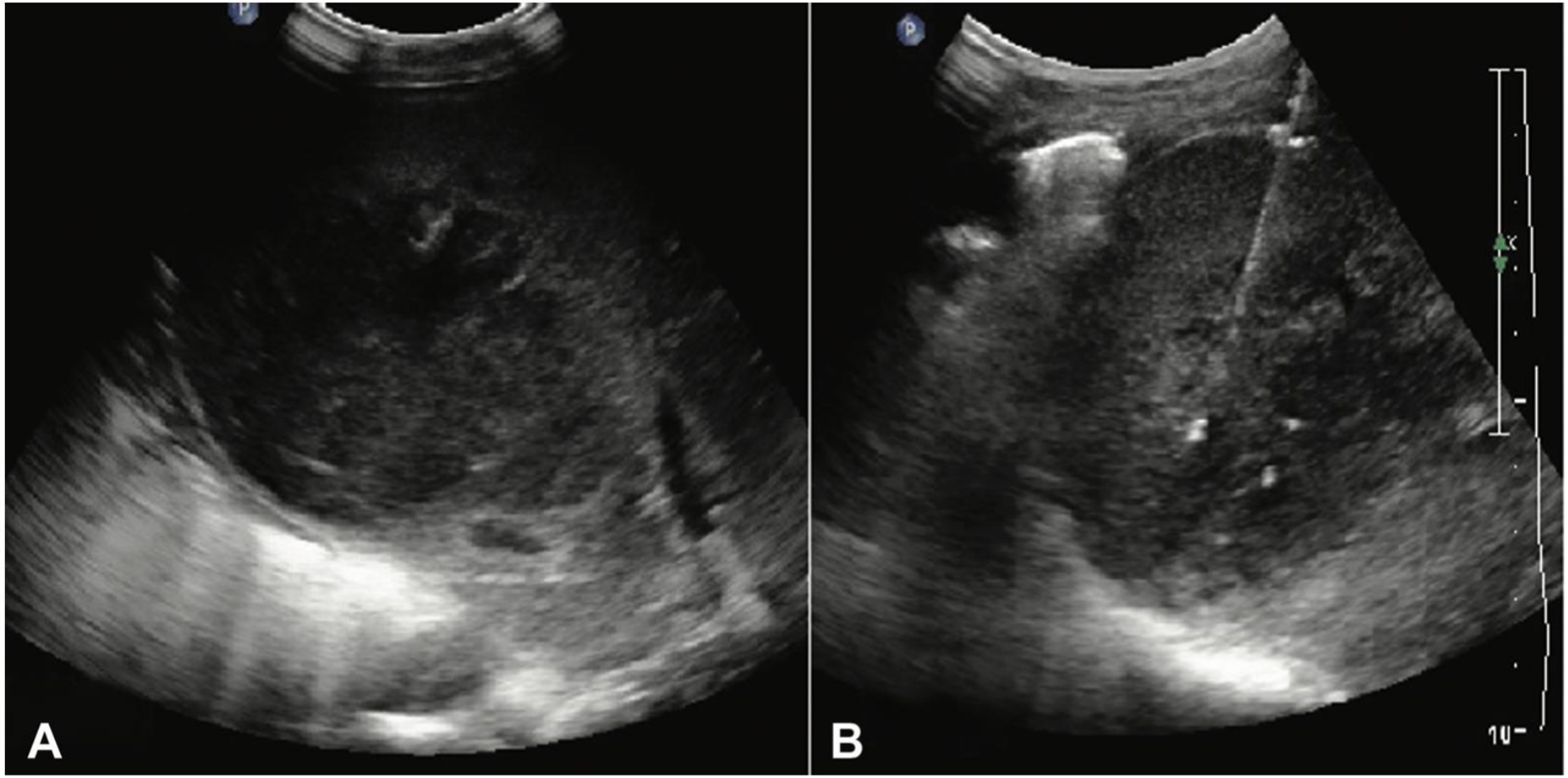
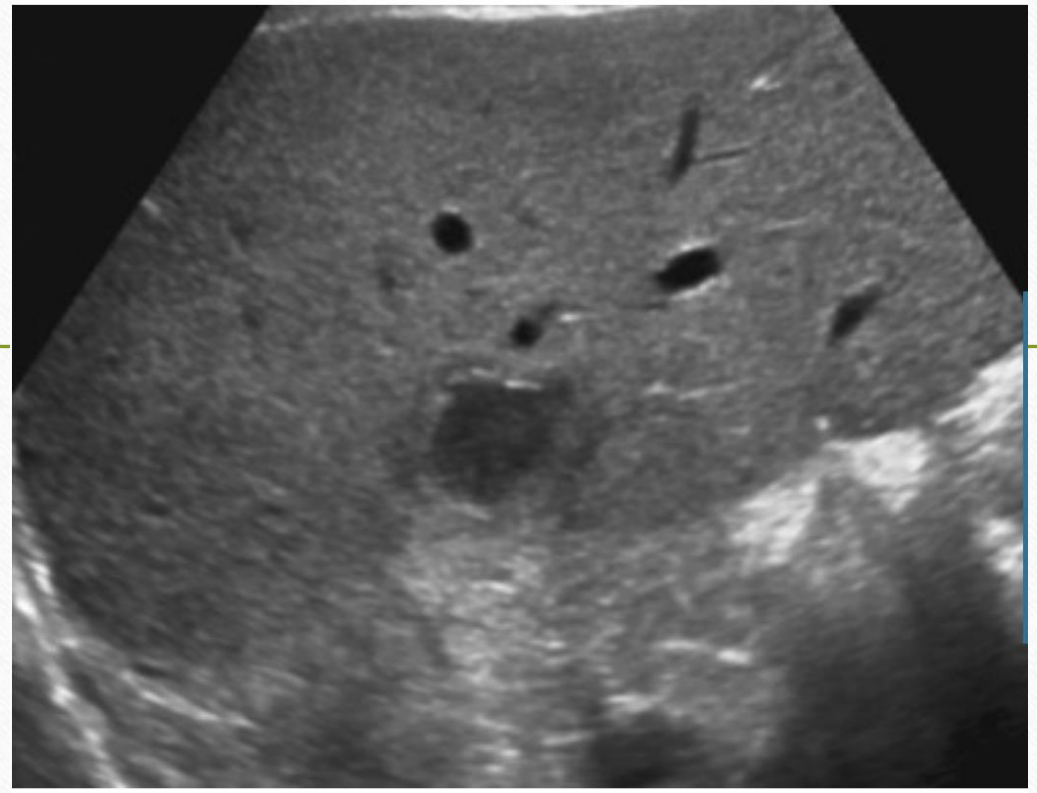
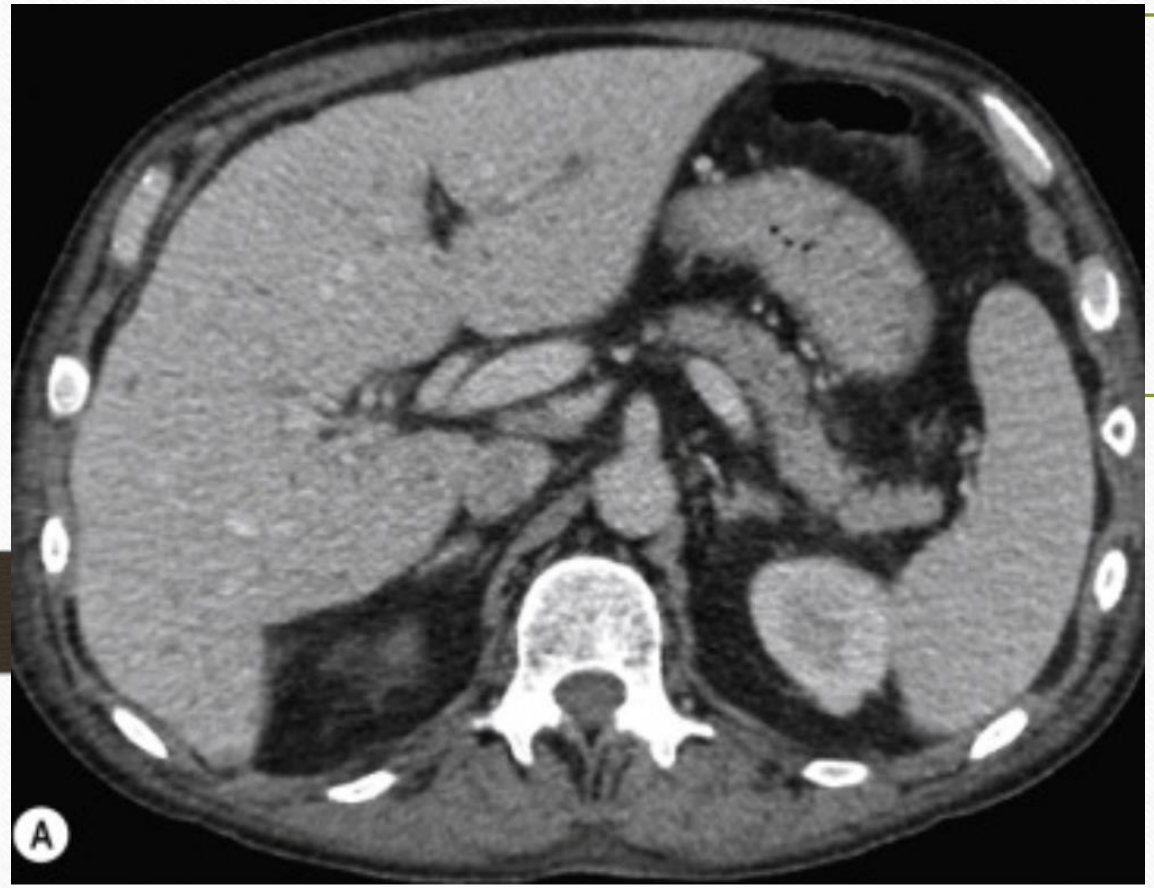


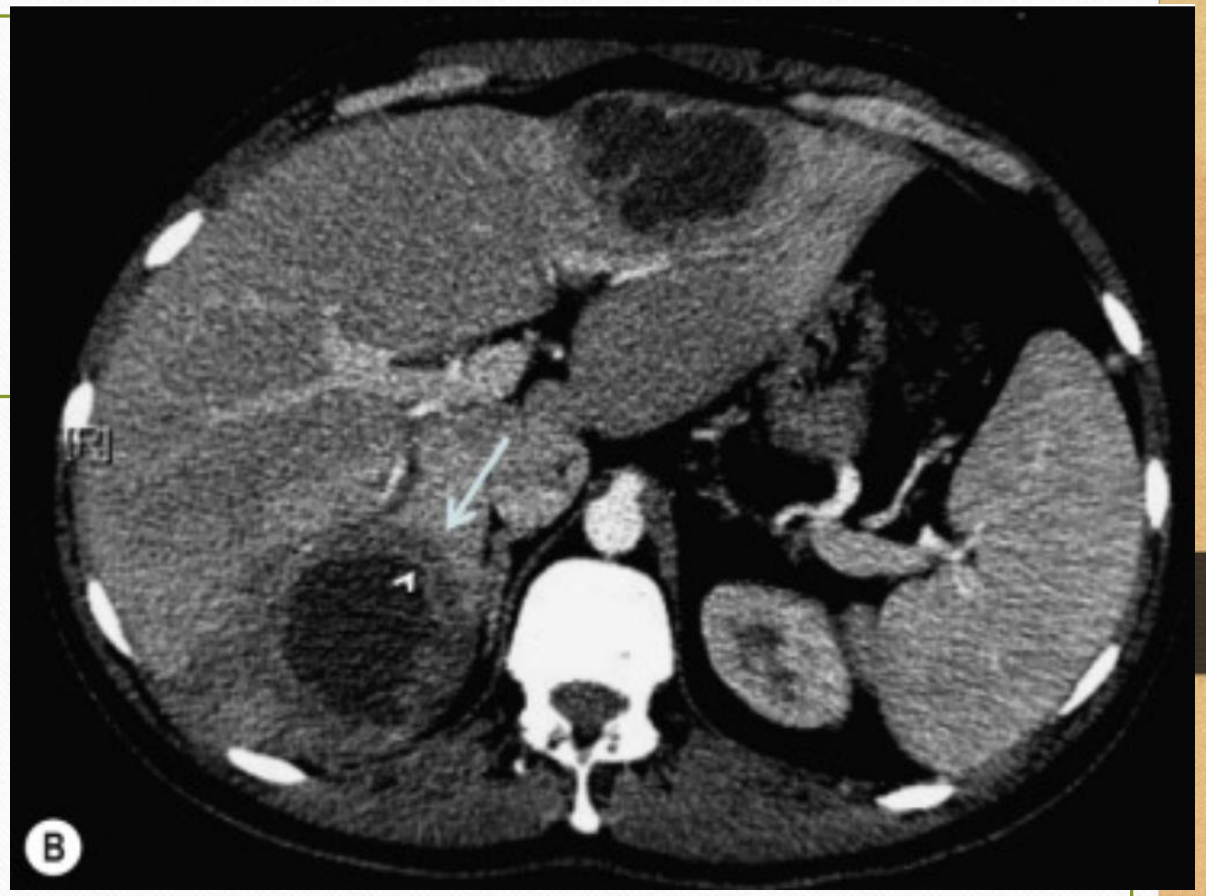
Fig. 1 Well-defined heterogeneously hypoechoic collection in the right lobe of liver suggestive of liver abscess (**A**) with pigtail in situ (**B**).



Echogenic thin inner membrane and hypoechoic perifocal oedema. Filled with hypo to anechoic material that causes posterior acoustic enhancement



CT portal phase: Multiple low attenuation lesions (pt with AML)



2 x Klebsiella abscesses. "double rim" sign- thin abscess membrane surrounded by perifocal oedema

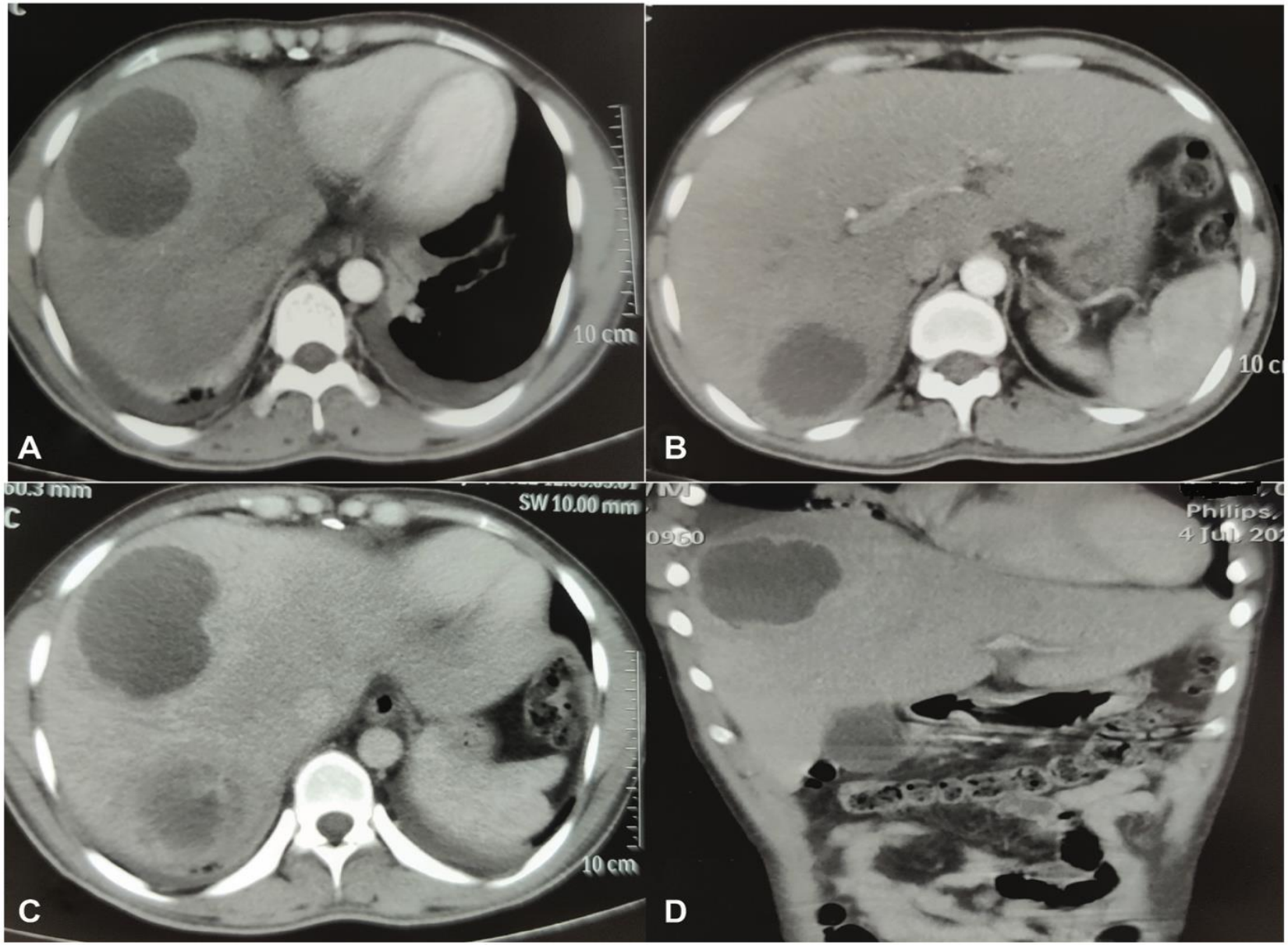


Fig. 2 Contrast-enhanced computed tomography of the abdomen showing peripherally enhancing hypodense lesions with shaggy margins and perilesional edema in the right lobe of the liver in the subcapsular region (**A**, **C**, **D**) suggestive of a liver abscess (**B**).

Medical Management

- <3-4cm: antibiotics(success rate close to 100%)
- IV 2-3 weeks, then oral 4-8 weeks
- Duration→ clinical and radiological response
- Empiric antibiotics should be directed against organisms typically responsible for causing liver abscess, covering gram-positive cocci, aerobic gram-negative bacilli, and anaerobes.
- ***IV ceftriaxone 2 g daily) + metronidazole tds***
- *IV piperacillin and tazobactam (4.5 gram every 6 h) + metronidazole*
- *IV ampicillin (2-g every 4–6 h) + gentamicin (5– 7 mg/kg) + metronidazole*
- *IV carbapenem + metronidazole*
- If suspicion of Staphylococcus aureus is high→vancomycin (15–20 mg/kg)

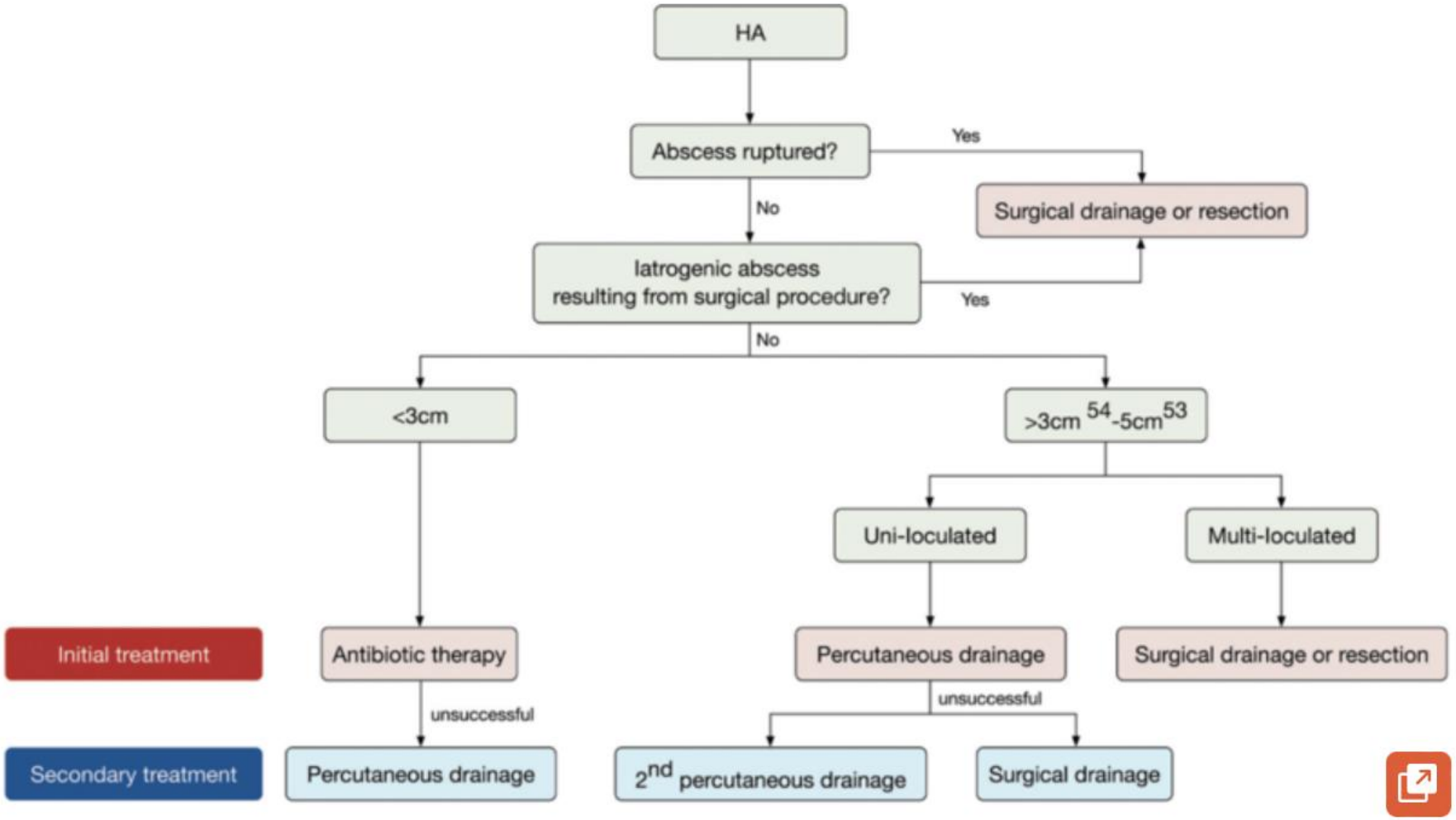
Drainage

- Percutaneous drainage if no response after 5-6 days
- Single time needle aspiration <catheter drainage
- Success rate 68 versus 100% if >5cm, shorter hospital stay
- Keep in until minimal drainage
- Drainage preferred for giant abscesses (>10cm), multiple abscesses, left lobe, large with impending rupture-like thinned out parenchyma at the periphery.

Surgical

- Abscesses >5cm: treatment failure percutaneous drainage> than surgery.
- No differences in complication rates or mortality.
- In cases with multiple or multiloculated abscesses-> individualise (number, size, and accessibility of abscesses)
- Peritonitis, abscess rupture, large abscess at a difficult anatomical site, or if the patient requires surgery for some other indication
- Laparoscopic surgery is a safe and viable alternative for patients requiring surgical drainage following failed medical or percutaneous treatment.

Management


HA
Abscess ruptured?
Yes
No
Surgical drainage or resection
Iatrogenic abscess resulting from surgical procedure?
Yes
No
<3cm
>3cm 54-5cm53
Uni-loculated
Multi-loculated
Initial treatment
Antibiotic therapy
Percutaneous drainage
Surgical drainage or resection
unsuccessful
unsuccessful
Secondary treatment
Percutaneous drainage
2nd percutaneous drainage
Surgical drainage

Amoebic abscess

- Entamoeba Histolytica
- Risk factors: alcoholism, pregnancy, malnutrition, old age, immunosuppression, steroid use, chronic infection
- History: Endemic areas, duration<14 days, history of dysentery during the last few months, fever, abdominal pain
- Symptoms of abdominal pain, malaise, LOA, sweating, LOW, fever. If rupture into pleural cavity: cough, chest pain

Amoebic abscess

- US (GOLD STANDARD) :
  - homogenous hypoechoic areas that can be single or multiple with round edges
  - variable size (around 2-6 cm in diameter)
  - incomplete rim of oedema
  - location near liver capsule,
  - internal septations (30%)
- Management: Non-complicated abscesses: Metronidazole, Paromomycin
- Percutaneous needle aspiration > surgery
- Address social factors

Table 3- Uncommon causes of hepatic abscesses

Rare pathogens that can cause hepatic abscesses	Important considerations
Mycobacterium	• Rare • Generally manifests as multiple abscesses • Consider this in patients at risk or with previous exposure who do not have typical pyogenic organisms on liver aspirate culture
Candida	• Think about this in patients with hematologic malignancies or other immunosuppressive conditions • Can also be a co-pathogen with other bacterial organisms
Fasciola	• Endemic in central and South America, Europe, Asia, Africa and Middle East, with sheep and cattle as the main hosts • Morbidity is proportional to fluke burden • Chronic phase can be asymptomatic or present with RUQ pain, nausea, vomiting, jaundice or pancreatitis • Diagnosis can be made with duodenal aspirates, eggs in stool or bile specimens • Diagnostic clues include eosinophilia, abnormal liver chemistries and anemia

Adapted from: Davis J, McDonald M. Pyogenic liver abscess. UpToDate. Sep 2020. and Leder K, Weller P. Liver flukes:fascioliasis. UpToDate. Sept 2020

SUMMARY

Table 2: Clinical and sonar characteristics of cystic lesions of the liver

Cystic lesion	Clinical Profile	Bloods/Cyst Fluid	Ultrasound
Non infective			
Simple Cyst	Vague RUQ pain Incidental	Non specific	Single or Multiple Well circumscribed anechoic structure with enhancement of the posterior wall
Biliary MCN	Epigastric or RUQ pain Palpable mass Could be asymptomatic Middle age females	Non specific Unlike MCN's of pancreas – aspiration not helpful	Single Anechoic mass with occasional internal septations or papillary projections
Polycystic disease	Generally asymptomatic. RUQ pain.	Renal dysfunction if kidneys involved	Multiple Hypoechoic, thin-walled cysts of varying sizes
Biliary Hamartoma (Von Meyenburg complex)	Mostly asymptomatic, incidental	Non specific	Multiple Variable because of the small lesion size Cysts might appear anechoic, hypoechoic, or hyperechoic
Infective – Parasitic			
Hydatid (echinococcal cyst)	Endemic area Asymptomatic or RUQ pain Hepatomegaly Occasionally jaundice	Positive Serology (False negative in 20%)	Multiple or Single Purely cystic to solid-appearing masses. "Water lily sign" wavy bands of delaminated endocyst. Daughter cyst or echogenic debris – "hydatid sand"
Pyogenic abscess	Pyrexia, rigors Severe RUQ pain Weight loss Systemically unwell	Elevated infective markers (WCC) Positive cyst and/or blood cultures	Single or Multiple Anechoic mass with well-defined or indistinct borders and may possibly contain echogenic debris or gas
Amoebic abscess	Endemic area High fever Severe RUQ pain	ELISA Positive (90% sensitivity) Typical "anchovy paste" appearance of abscess content	Single or Multiple Hypoechoic round or oval lesions located close to the liver capsule that show low-level internal echoes and posterior acoustic enhancement
Caroli's disease	Recurrent attacks of RUQ pain Cholangitis	Non specific	Multiple of varying size Dilated cystic structures of communicate with the biliary tree

Kloppers et al, South African Gastroenterology Review, 2016

SUMMARY

Table 3: CT and MRI characteristics of cystic liver lesions

Cystic lesion	CT	MRI \ MRCP
Simple Cyst	Well-defined Attenuation (0–15 HU) similar to water No enhancement with contrast	Well-defined T1: hypointense T2: hyperintense
Biliary MCN	Complex solitary well-defined, multilocular, intrahepatic cystic lesion. Occasional upstream bile duct dilatation Internal septations Enhancement of walls	Multilocular mass Septated Homogeneous high (T2) signal intensity
Polycystic disease	Typically appear to be multiple simple cysts on imaging	T1: Very low signal intensity T2: Homogeneous high signal intensity
Biliary Hamartoma (Von Meyenburg complex)	Multiple, small (< 15 mm), round or irregular scattered cysts with a predilection for the subcapsular region	MRI Multiple, tiny cystic lesions with irregular borders MRCP - no biliary communication
Caroli's disease	Cystic and usually have a central enhancing component, the "central dot" sign, which is the portal radicle.	MRCP demonstrates communication between the Caroli's cysts and the biliary tee
Hydatid (echinococcal cyst)	Well-defined, hypo-attenuating lesion with a distinguishable wall Daughter cyst identified in majority Calcification in mature cysts	T2 sequence: Pericyst has a hypointense rim Hydatid debris is markedly hyperintense Daughter cysts are hypointense
Pyogenic abscess	Iso- to hypo-attenuating compared with background liver on the unenhanced phase Peripheral rim of enhancement on IV contrast	Variable signal intensity Peri-lesional oedema
Amoebic abscess	Lesions with slightly higher attenuation than water Smooth or nodular borders Thick wall that typically enhances	The central portion of the lesion appears cystic The ring exhibits variable intensities on T1- and T2-weighted imaging

Kloppers et al, South African Gastroenterology Review, 2016

Take home message

- Liver cysts have a variety of presentations
- The vast majority are benign
- TAG72 can help differentiate simple cyst from MCN
- Ultrasound is imaging of choice in simple, CT/MRI if complicated
- Most require a symptomatic approach
- Individualise management
- NB to identify premalignant cysts

Thank you!!

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