



Hilar cholangiocarcinoma (H-CCC)

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Epidemiology and risk factors

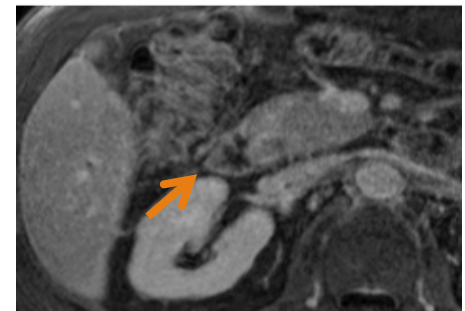
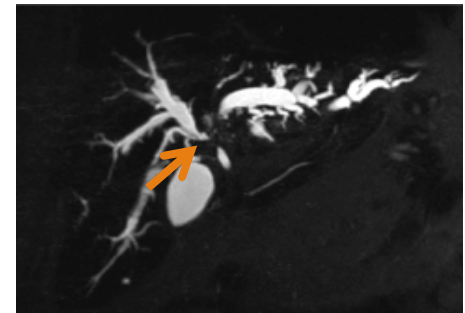
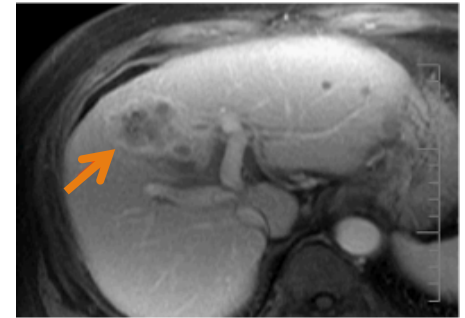
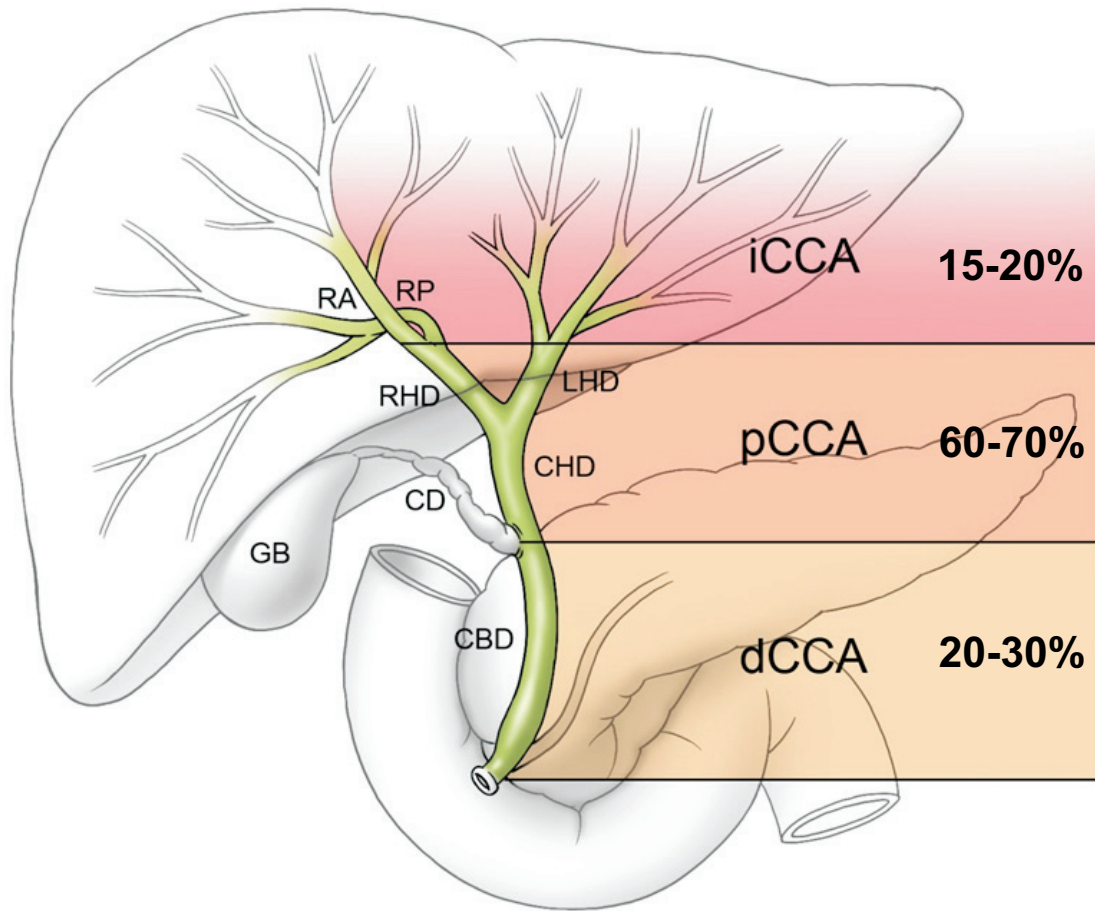
- 15% of hepatic and <3% of GIT tumours
- Incidence 1.2-3.3 per 100 000 in population
- Incidence seems to stable - ↑ I-CCA; ↓ H-CCA
- Increasing incidence with age - 70% > 65 yrs
- Male predominance
- ↑ Hispanic and Asian populations

Epidemiology and risk factors

- Infestations
 - Clonorchis sinensis
 - Opistorchis viverini
 - Ascaris lumbricoides
- Recurrent pyogenic cholangitis
- Infection
 - HIV
 - HBV
 - HCV
 - EBV
- PSC
- IBD ?

- Diabetes
- Obesity
- Anomalies
 - PD junction anomalies
 - Choledochal cysts
- Ethanol overconsumption
- Bilio-enteric drainage procedures
- Toxins
 - Dioxin
 - Thorotrast
 - PVC

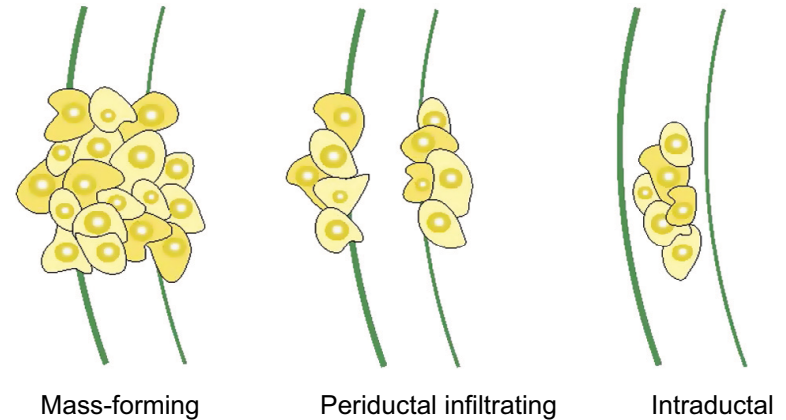
Classification - anatomic



Classification - pathologic

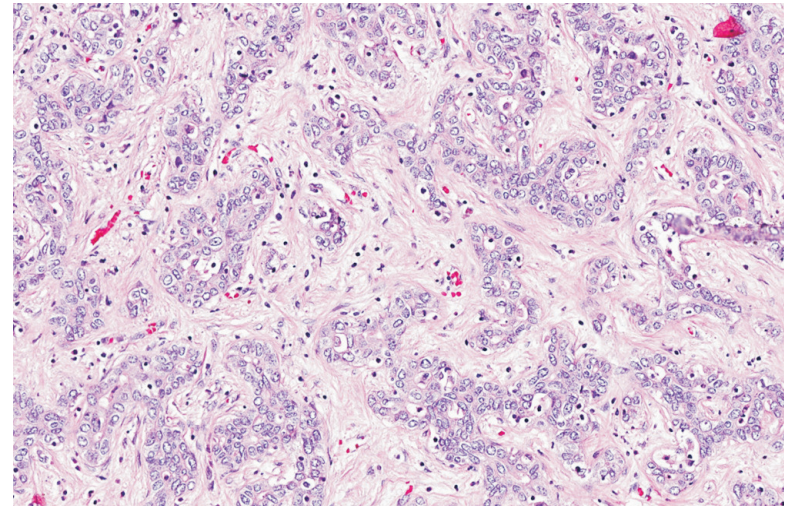
Macroscopic

- mass-forming
- periductal-infiltrating
- intraductal-papillary



Histopathology

- 90-95% adenocarcinomas
- moderate to poor differentiation
- mucin expression is common
- desmoplastic stroma
- CK7 and CK19 expression



Presentation

- Clinical
 - Early symptoms non-specific.
 - Abdominal pain or discomfort,
 - Anorexia,
 - Weight loss
 - Pruritus
 - Jaundice – only for complete obstruction
 - Cholangitis is uncommon (30% have bacteremia).
- Incidental
 - Abnormalities on routine blood testing
 - Imaging
- Screening - PSC

Diagnosis and work-up

- Diagnosing
- Staging
- Assessing resectability

Differential diagnosis of a hilar stricture

- (A) Dominant stricture in PSC
- (B) Hepatolithiasis and recurrent pyogenic cholangitis
- (C) Mirizzi syndrome
- (D) Inflammatory-infiltrative
 - (a) Inflammatory pseudotumour
 - (b) IgG4 related Cholangiopathy
 - (c) Eosinophilic cholangiopathy
 - (d) Follicular cholangiopathy
 - (e) Xanthogranulomatous cholangitis
 - (f) Mast cell cholangiopathy
 - (g) Sarcoidosis
- (E) Infective
 - (a) Cholangiopathy in the immunocompromised
 - (i) AIDS cholangiopathy
 - (ii) Primary immunodeficiency
 - (b) Bacterial
 - (c) Biliary tuberculosis
 - (d) Fungal
 - (e) Parasitic
- (F) Vascular
 - (a) Portal hypertensive biliopathy
 - (b) Ischaemic cholangiopathy
- (G) Toxic
 - (a) Postchemotherapy
 - (b) Thorotrast-induced granuloma
- (H) Trauma
 - (a) Biliary
 - (b) Systemic
- (I) Tumours
 - (a) Malignant
 - (i) Gall bladder carcinoma
 - (ii) Hepatocellular carcinoma
 - (iii) Lymphoepithelioma-like carcinoma
 - (iv) Neuroendocrine tumours
 - (v) Granular cell tumour
 - (vi) Lymphoma
 - (vii) Leukemia
 - (viii) Myeloma
 - (ix) Other metastasis
 - (b) Benign
 - (i) Neurilemmoma
- (J) Miscellaneous
 - (a) Proliferative cholangitis
 - (b) Nonparasitic cysts
 - (c) Erdheim-Chester disease
 - (d) Ormond's disease
 - (e) Heterotopic pancreas/stomach
 - (f) Cholecystohepatic duct with absent common hepatic duct
- (K) Idiopathic

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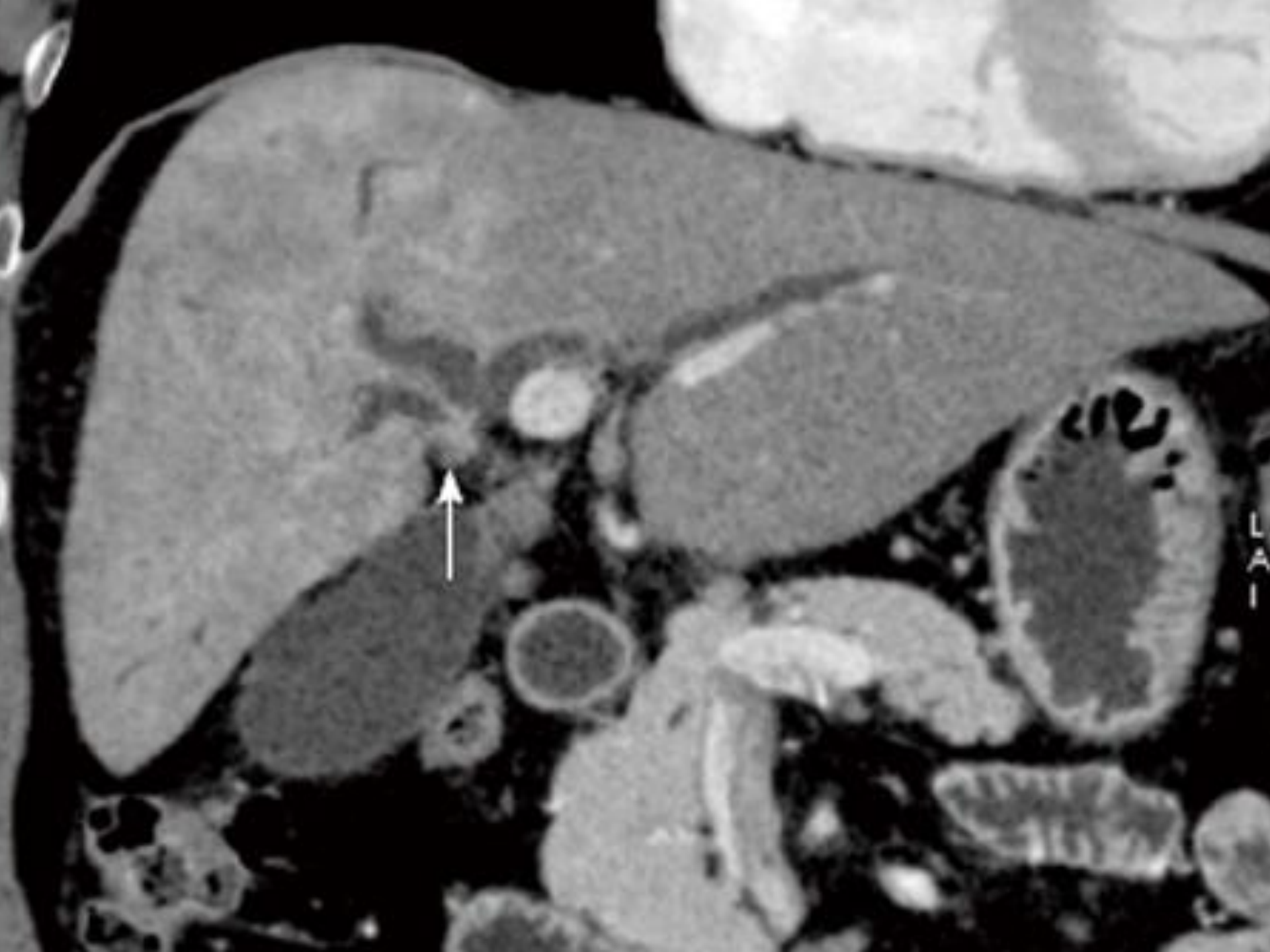
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- Gallbladder carcinoma

Diagnosis - imaging

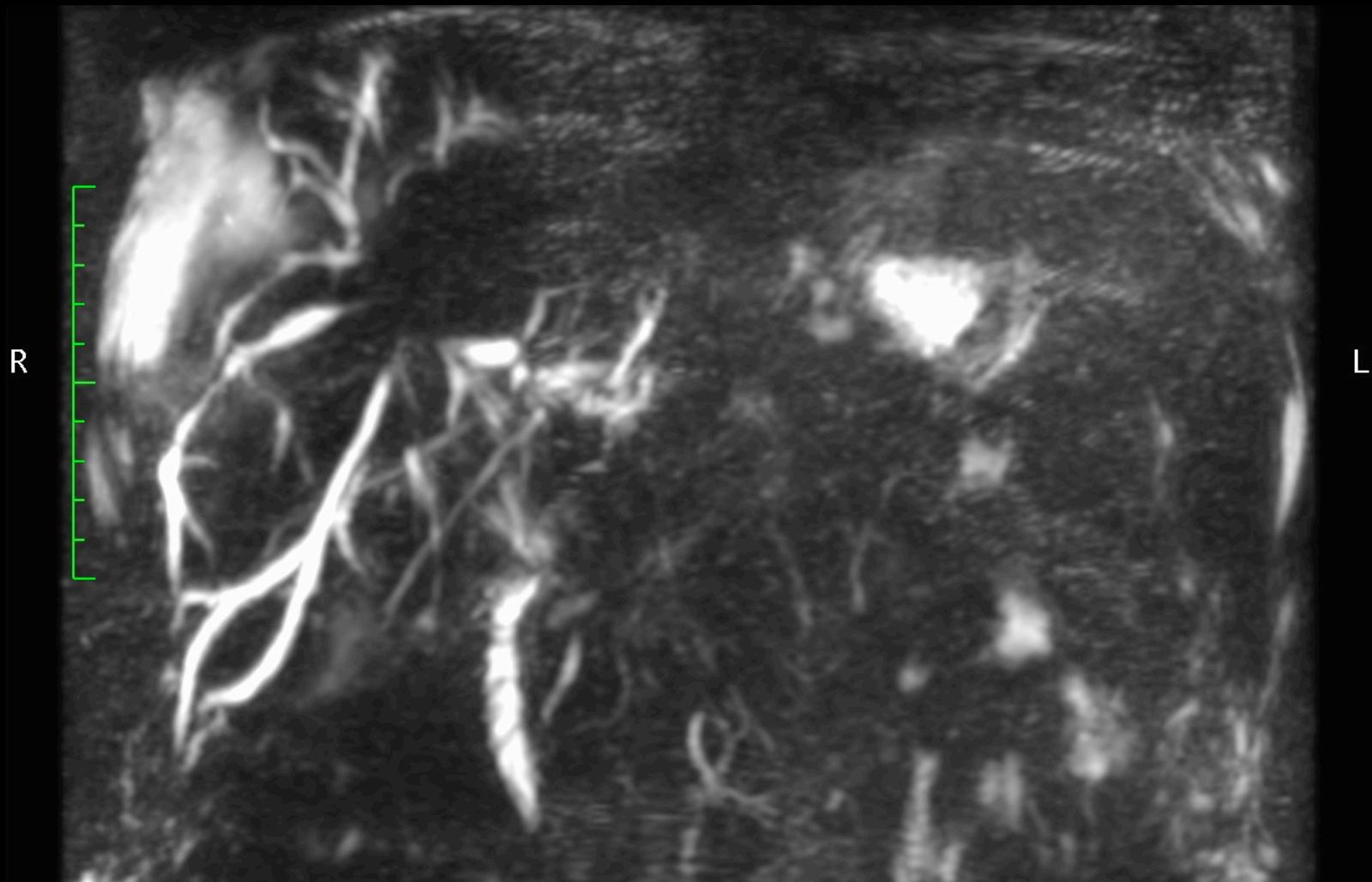
- Tumour
- Liver
- Bile ducts

Options

- Tumour/liver - CE-US, CE-CT, CE-MRI
- Bile ducts – MRCP/ERCP/PTC

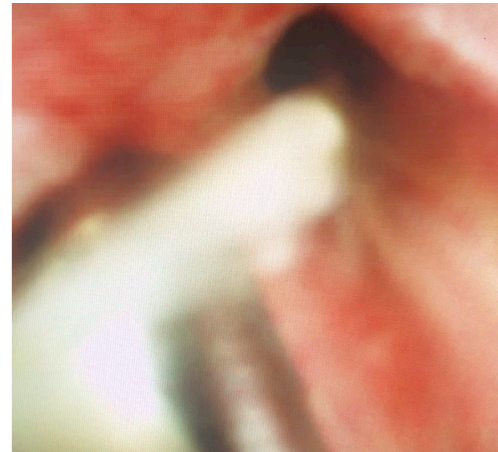
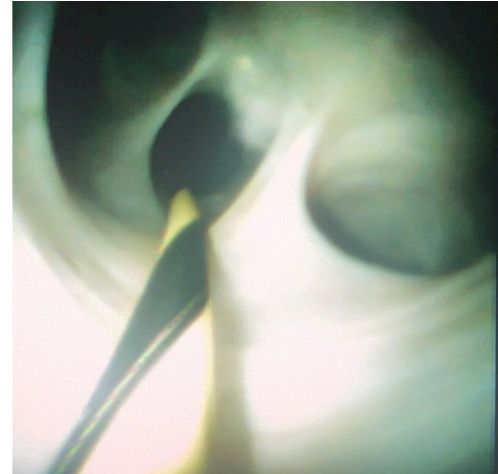






Diagnosis - pathology

- Brush cytology
- Cholangioscopy + biopsies

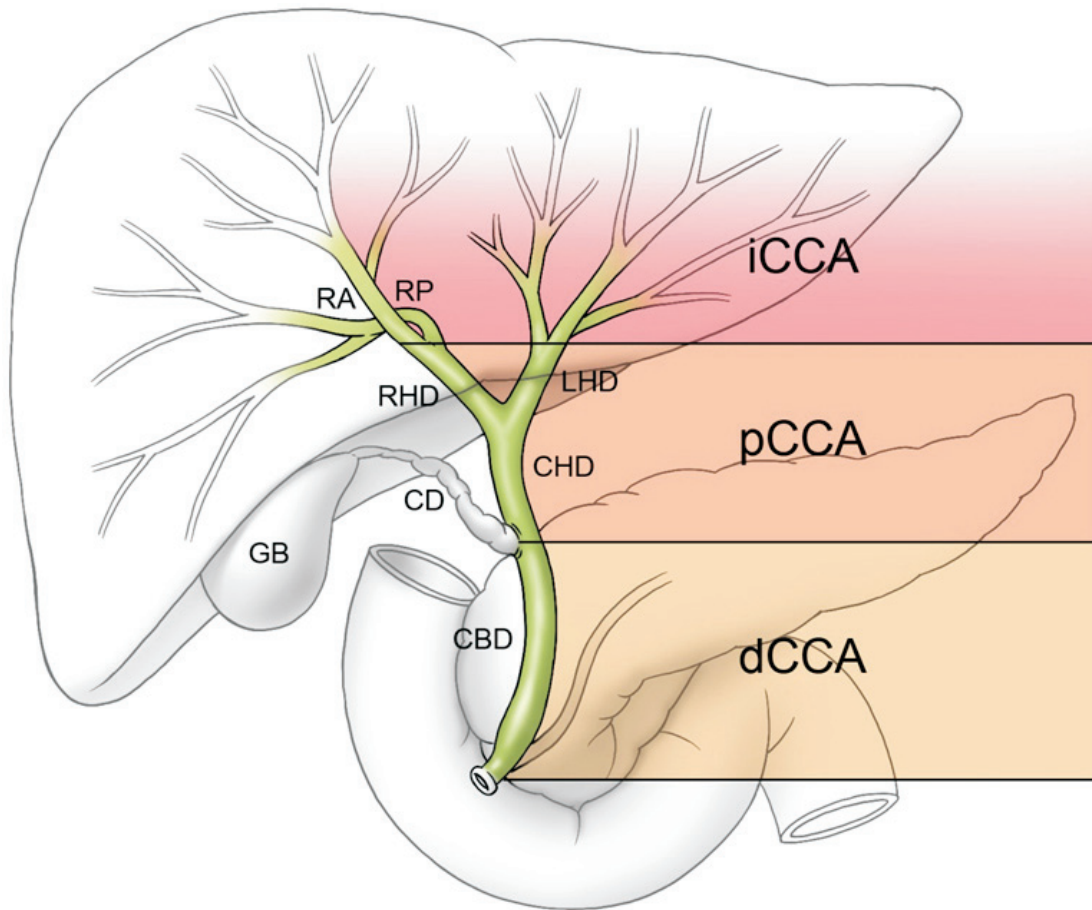


	Sensitivity	Specificity
Brush cytology	~ 45%	~ 80%
Biopsy	~ 55%	~ 90%

Staging - AJCC 8th Edition

	dCCA	pCCA	iCCA
Primary tumour (T)			
TX	Primary tumour cannot be assessed	Primary tumour cannot be assessed	Primary tumour cannot be assessed
T0	n/a	No evidence of primary tumour	No evidence of primary tumour
Tis	Carcinoma in situ/high-grade dysplasia	Carcinoma in situ/high-grade dysplasia	Carcinoma in situ (intraductal tumour)
T1	Tumour invades the bile duct wall with a depth <5 mm	Tumour confined to the bile duct, with extension up to the muscle layer fibrous tissue	–
T1a	–	–	Solitary tumour ≤5 cm without vascular invasion
T1b	–	–	Solitary tumour >5 cm without vascular invasion
T2	Tumour invades the bile duct wall with a depth of 5-12 mm	Tumour invades beyond the wall of the bile duct to surrounding adipose tissue, tumour invades adjacent hepatic parenchyma	Solitary tumour with intrahepatic vascular invasion or multiple tumours (with or without vascular invasion)
T2a	–	Tumour invades beyond the wall of the bile duct to surrounding adipose tissue	–
T2b	–	Tumour invades adjacent hepatic parenchyma	–
T3	Tumour invades the bile duct wall with a depth >12 mm	Tumour invades unilateral branches of the portal vein hepatic artery	Tumour perforating the visceral peritoneum
T4	Tumour involves the celiac axis, superior mesenteric artery, and/ common hepatic artery	Tumour invades the main portal vein, its branches bilaterally, the common hepatic artery; unilateral second-der biliary radicals with contralateral portal vein hepatic artery involvement	Tumour involving local extrahepatic structures by direct invasion
Regional lymph nodes (N)			
NX	Regional lymph nodes cannot be assessed	Regional lymph nodes cannot be assessed	Regional lymph nodes cannot be assessed
N0	No regional lymph node metastasis	No regional lymph node metastasis	No regional lymph node metastasis
N1	Metastasis in one to three regional lymph nodes	One to three positive lymph nodes typically involving the hilar, cystic duct, common bile duct, hepatic artery, posterior pancreatoduodenal, and portal vein lymph nodes	Regional lymph node metastasis present
N2	Metastasis in four or more regional lymph nodes	Four or more positive lymph nodes from the sites described for N1	–
Distant metastasis (M)			
M0	No distant metastasis	No distant metastasis	No distant metastasis
M1	Distant metastasis	Distant metastasis	Distant metastasis present

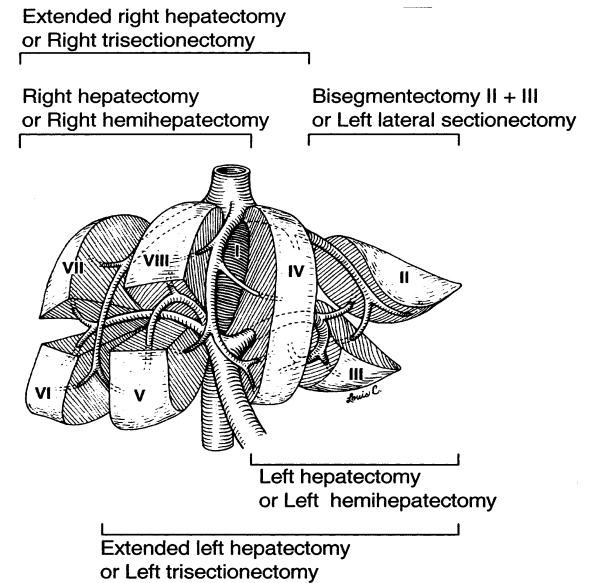
Defining resectability



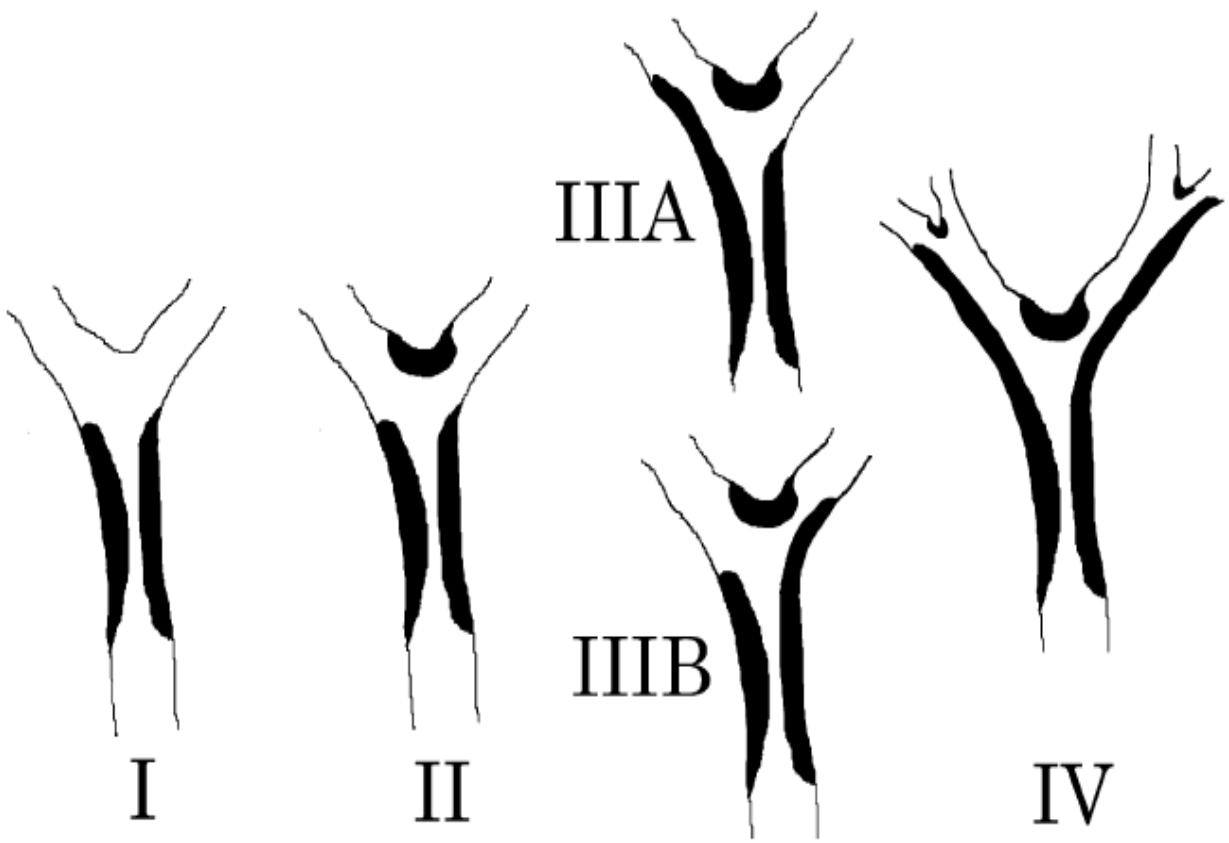
Sufficient FLR
R0 resection

The future liver remnant

- Sufficient volume and quality
 - to sustain immediate post-operative function
 - to allow sufficient post-resection regeneration
- Intact arterial and portal supply and biliary and venous drainage



Bismuth-Corlette classification for hilar CCC



The descriptions correlate with the operations required for R0 resection and establishment of biliary continuity

Detailed local staging required

- Bile duct involvement
 - ERCP
 - MRCP
 - PTC
- Vascular involvement (arterial and venous)
 - CE-MDCT
 - MRI

Specific contraindications for surgery

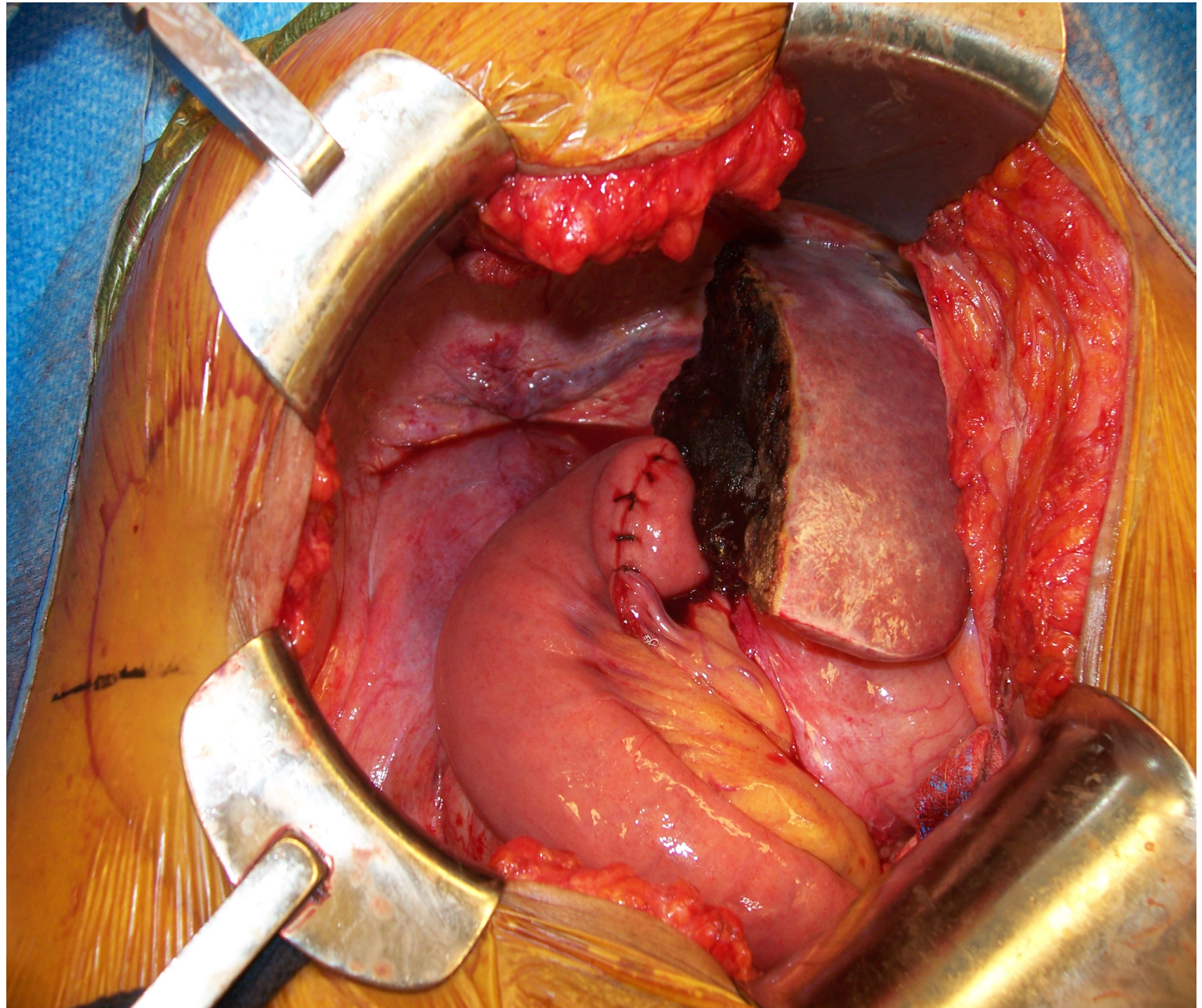
- Bilateral extension of tumour to secondary biliary radicles
- Main portal vein encasement or occlusion proximal to its bifurcation
- Unilateral tumor extension to secondary bile ducts with contralateral vascular encasement/occlusion
- Atrophy of one hemi-liver with contralateral vascular encasement or secondary biliary extension

Surgical components

- Resection of affected bile ducts
- Resection of the extrahepatic bile ducts
- Lymph node dissection in hepatoduodenal ligament
- Cholecystectomy
- Liver resection (including routine resection of segment 1)

Resection results – H-CCC

Author (year)	n	Concomitant Liver Resection (%)	% R0 Resection	5-year Survival (%)
Cameron (1990)	39	20	15	8
Gerhards (2000)	112	29	14	-
Su (1996)	49	57	24	15
Hadjis (1990)	27	60	56	22
Jarnagin (2001)	80	78	78	27
Klempnauer (1997)	147	79	79	28
Neuhaus (1999)	95	85	61	22
Kosuge (1999)	65	88	88	33
Nimura (1990)	55	98	83	40



Controversies

- PET
- Pre-operative biliary drainage
- Laparoscopy
- Volume manipulation
- Transplantation

PET

- Low sensitivity - false negatives due to low volume metastases
- Reasonable specificity - false positives due to stents or recent cholecystectomy

Pre-operative biliary drainage

- ERCP vs. PTC
- Unilateral or bilateral
- Routine vs. selective for FLR
- Plastic vs. metal

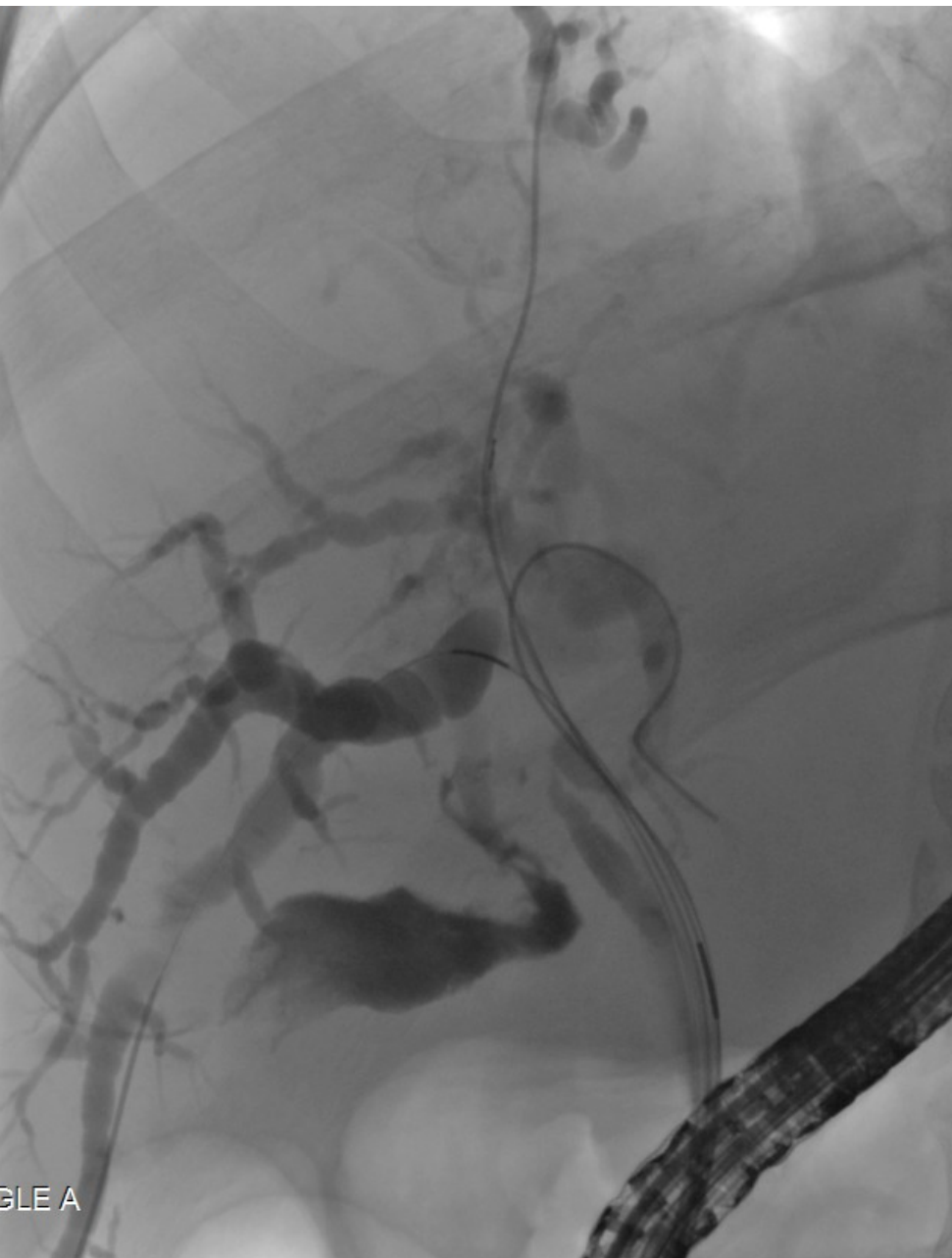
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Endoscopic versus percutaneous biliary drainage in patients with resectable perihilar cholangiocarcinoma: a multicentre, randomised controlled trial



- Endoscopic (n=27) or PTC (n=27).
- Severe drainage-related complications:
PTC=17 (63%) vs. endoscopic = 18 (67%)
- Mortality: PTC = 11 (41%) vs. 3 (11%)



BLE A



BLE A

Pre-operative biliary drainage

- ERCP vs. PTC
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Pre-operative biliary drainage

- ERCP vs. PTC
- Unilateral or bilateral
- **Routine vs. selective for FLR**
- Plastic vs. metal

Current approach

Drainage of the FLR only if:

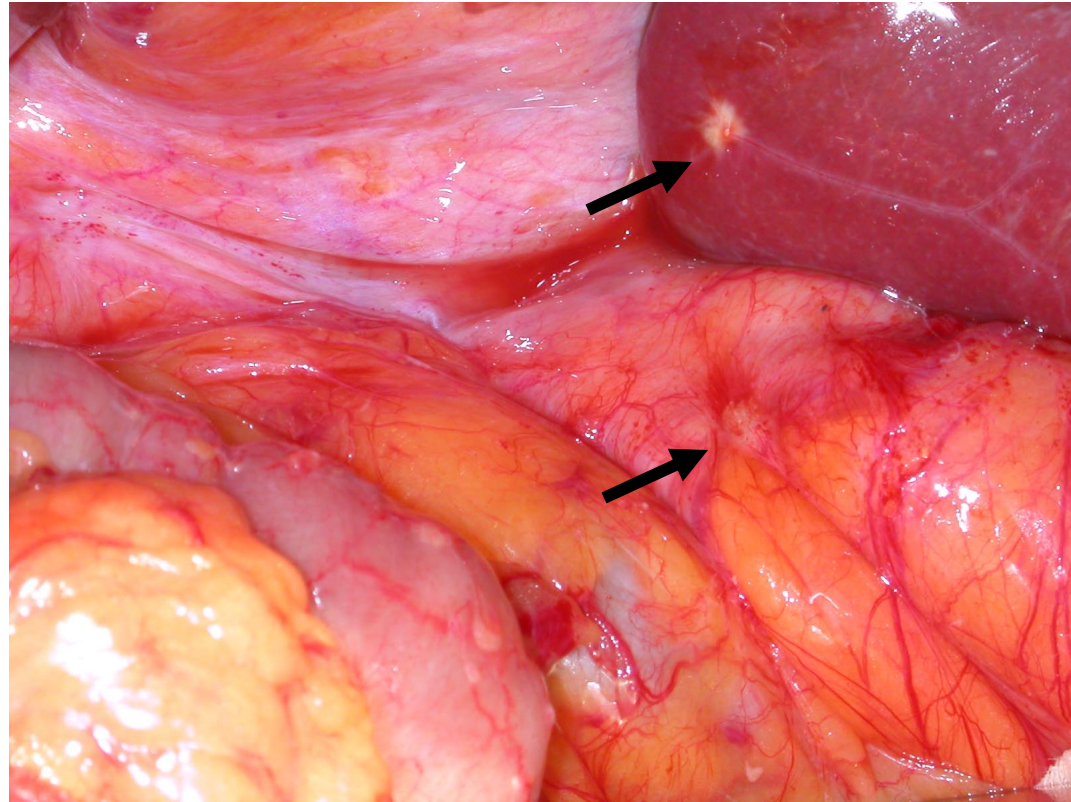
- cholangitis
- bilirubin level exceeding 350 $\mu\text{mol/L}$
- FLR below 40%.

Pre-operative biliary drainage

- ERCP vs. PTC
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- Routine vs. selective for FLR
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Laparoscopy – selective vs. routine

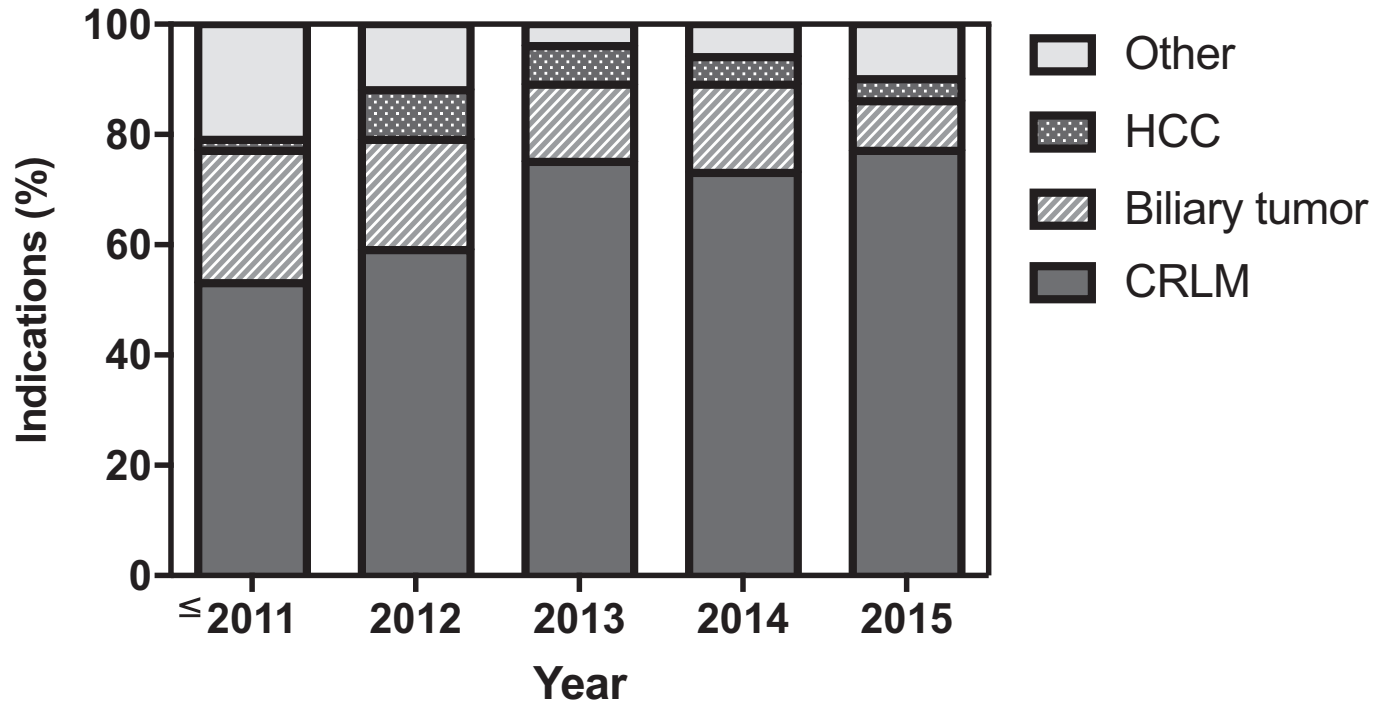
- High CA 19-9
- Extensive tumour
- Suspicion of peritoneal metastases



Pre-operative biliary drainage

- ERCP vs. PTC
- Unilateral or bilateral
- Routine vs. selective for FLR
- Plastic vs. metal

Volume manipulation PVE/PVL vs ALPPS



ALPPS versus conventional surgery

- ALPPS registry and MSKCC/AMC cohorts
- 90 day mortality 48% vs. 28%
- median OS 6 vs. 27 months

Liver transplant

- Contraindicated for intrahepatic CCC
- Experimental for hilar CCC
- With rigorous patient selection 5-year recurrence-free survival 65–70%
- Neo-adjuvant treatment pre-transplant
 - external beam radiotherapy (EBRT) - 4500 cGy
 - continuous infusion of 5-FU during EBRT
 - brachytherapy boost - trans-catheter Iridium-192
 - Xeloda for 2 weeks in every 3-week period until transplantation

ASCO special article

Adjuvant Therapy for Resected Biliary Tract Cancer: ASCO Clinical Practice Guideline

Rachna T. Shroff, MD¹; Erin B. Kennedy, MHSc²; Melinda Bachini³; Tarios Bekaii-Saab, MD⁴; Christopher Crane, MD⁵; Julien Edeline, MD, PhD⁶; Anthony El-Khoueiry, MD⁷; Mary Feng, MD⁸; Matthew H.G. Katz, MD⁹; John Primrose, MD¹⁰; Heloisa P. Soares, MD, PhD¹¹; Juan Valle, MD¹²; and Shishir K. Maithel, MD¹³

- All patients - adjuvant capecitabine for a duration of 6 months
- Extrahepatic cholangiocarcinoma and an R1 resection - may be offered chemoradiation

Thank you

