Cholangiocarcinoma

Clinical diagnosis, staging, resectability and surgical management

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Learning framework

1. Classification

iCCA • pCCA • dCCA
Anatomic origin drives imaging and management.

2. Diagnosis

Cross-sectional imaging → tissue acquisition when indicated → MDT decision.

3. Resectability

Vascular, biliary, nodal and metastatic disease + patient fitness.

4. Surgical planning

R0 resection, future liver remnant, biliary drainage, portal vein strategies.

5. Outcomes

Post-hepatectomy liver failure, lymphadenectomy, transplantation and adjuvant therapy.

Anatomic classification

Intrahepatic CCA (iCCA)

Arises within liver parenchyma, proximal to the second-order bile ducts.

Second most common primary liver cancer globally after HCC.

Perihilar CCA (pCCA)

Located between the second-degree bile ducts and cystic duct insertion into the common bile duct.

pCCA + dCCA = extrahepatic CCA.

Distal CCA (dCCA)

Confined to the common bile duct below the cystic duct insertion.

Distal strictures often require EUS/ERCP-based tissue acquisition.

Historical distribution: pCCA ~50–60%; iCCA <20%.

iCCA may be an incidental finding in ~20% of cases.

Aetiology and clinical presentation

Risk factors

Major known risk factors are associated with chronic biliary epithelial inflammation and bile stasis.

Examples highlighted in the source: primary sclerosing cholangitis (PSC) and liver flukes.

Clinical spectrum

- Abnormal liver function tests
- Jaundice and abdominal pain
- Tiredness/lethargy
- Anorexia and weight loss
- Thromboembolic disease
- Hypercalcaemia / paraneoplastic syndromes
- Abdominal mass or distant organ infiltration
- Malignant adenopathy, pleural disease, ascites
- Fever of unknown origin

Why cholangiocarcinoma surgery is different

The central question is no longer simply “Can I remove the tumor?”

1 ONCOLOGIC CLEARANCE

2 FUTURE LIVER REMNANT

3 TUMOR BIOLOGY

R0 resection remains the only established potentially curative surgical strategy.

Major hepatectomy may be required for perihilar disease; PHLF is the key technical threat.

In iCCA, margin width, nodal status, multifocality and molecular subtype influence the value of aggressive surgery.

Modern decisions require surgery + interventional radiology + GI/endoscopy + oncology + pathology.

Imaging & Staging

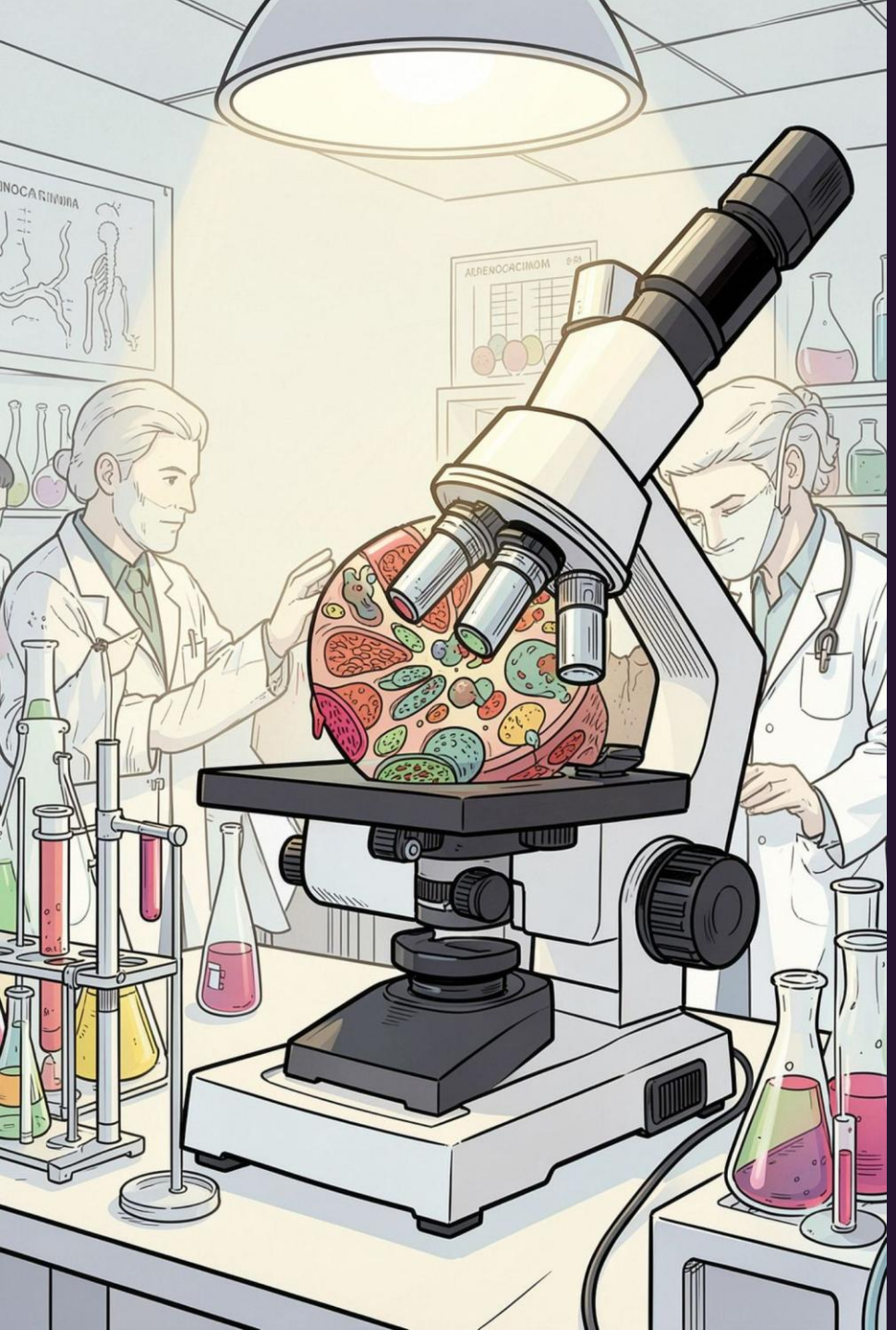


Key Modalities

- **MRI + MRCP** — superior to CT for assessing biliary obstruction level and extent; essential for perihilar and intrahepatic tumors
- **CT** — multiphasic contrast-enhanced CT for vascular involvement and distant metastases; for distal eCCA, MRI adds little beyond CT
- **18FDG-PET CT** — recommended for nodal and distant metastatic disease detection and relapse confirmation
- **US/CT-guided biopsy** — for pathological diagnosis following MDT consensus

Staging must be performed **before** any biliary stent placement.

Made with GAMMA



Pathology

Large Duct Type

Arise near central ducts; grow along duct walls. Whiter and firmer than HCC due to stromal component.

Small Duct Type

Peripheral, white/grey mass-forming lesions in hepatic parenchyma. **CRP** is a highly specific marker for small duct iCCA.

IHC Use

Not routinely required. Useful when: (1) prior extrahepatic malignancy needs differentiation from CCA; (2) histology is equivocal between CCA and HCC.

Made with GAMMA

Endoscopic diagnosis: tailor the approach to anatomy

Distal CCA / malignant distal stricture

EUS with FNB/FNA + ERCP-directed brushings and stenting.

In non-jaundiced patients, EUS may precede the decision to proceed to ERCP.

Proximal / perihilar disease

Avoid sampling a potentially operable hilar/proximal mass because of possible peritoneal contamination and tumour seeding.

EUS can sample involved locoregional or metastatic nodes for staging.

Key pathology point

Biliary biomarkers are not recommended as a replacement for cytology/histology.

Diagnostic accuracy is imperfect; persistent uncertainty requires MDT discussion with the patient/family.

Preoperative biliary drainage

General principle

Routine drainage of preoperative hyperbilirubinaemia may increase postoperative complications. Benefit is more likely with intractable pruritus, cholangitis or organ dysfunction.

If drainage is required

ERCP with a fully covered metal stent for distal malignant obstruction; plastic stent(s) for proximal obstruction when surgery is expected to be delayed >4 weeks.

Operable pCCA

Discuss at an HPB treatment centre first. Consider unilateral drainage of the future remnant lobe.

Inoperable pCCA

Palliative stenting by ERCP or PTC; establish a monitoring pathway for recurrent stent blockage.

Preoperative biliary drainage: selective

WHY DRAIN?

Reduce cholestasis before major resection.

Treat cholangitis / optimize the intended FLR.

Potentially reduce post-hepatectomy liver failure in selected patients.

WHY NOT DRAIN EVERYONE?

Infection and cholangitis.

Tumor seeding risk, particularly with PTBD.

Drain malfunction, inflammation and prolonged delay may compromise surgery.

Supplied hilar review: a bilirubin target <5 mg/dL is desirable before major resection, but the evidence is heterogeneous and decisions are individualized.

Preoperative work-up: answer five questions

1. WHERE?

Multiphasic CT / MRI-MRCP
Define ductal & vascular anatomy

2. HOW FAR?

Liver, nodes, peritoneum,
extrahepatic metastases

3. CAN THE LIVER COPE?

FLR volume + functional assessment
± PVE/LVD

4. SHOULD WE DRAIN?

Selective biliary drainage when indicated
balance infection vs benefit

5. WHAT IS THE BIOLOGY?

Histology when needed + NGS
IDH1 / FGFR2 and other actionable alterations

Key point: a “resectable” scan is not enough — resectability is anatomical + functional + biological.

Preoperative management: practical checklist

Stage before any biliary stent placement.

Multiphasic contrast-enhanced CT chest/abdomen/pelvis: hepatic artery, portal vein and distant metastases.

Contrast MRI + MRCP: bile duct anatomy and longitudinal tumour extent.

In possible surgical candidates, EUS-guided sampling of lymph nodes can help exclude metastatic nodal disease.

All decisions should flow through an HPB multidisciplinary team.

Two surgical problems — two different anatomies

PERIHILAR (HILAR) CHOLANGIOCARCINOMA

Longitudinal ductal spread defines the operation.

Bismuth–Corlette describes ductal extent but does not fully capture vascular invasion, atrophy or metastasis.

R0 often requires major hepatectomy + caudate resection ± portal vein reconstruction.

Selected unresectable, non-metastatic disease may enter a transplant pathway.

INTRAHEPATIC CHOLANGIOCARCINOMA

Parenchymal tumor: resection strategy is driven by tumor location, vascular relationships and FLR.

R0 is crucial; ≥5–10 mm is a practical target when feasible.

Regional lymphadenectomy improves staging; therapeutic benefit remains unsettled.

Systemic therapy and molecular profiling increasingly influence conversion and perioperative strategy.

Surgery for pCCA, dCCA and iCCA

Perihilar CCA

R0 resection is the only curative treatment described.

Frequently requires:
- bile duct excision
- partial hepatectomy
- en bloc caudate lobectomy

to achieve negative margins.

Intrahepatic CCA

Preferred treatment is complete R0 resection with an adequate liver remnant.

Most patients with a single large tumour require (extended) hemi-hepatectomy.

Lymphadenectomy is recommended in resectable iCCA.

Hepatic resection

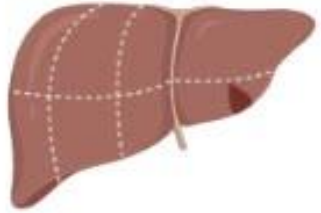
- **in type I and II HC**:
- Although the literature is inconclusive, parenchyma preserving hepatic resections like central hepatectomy in type I and II HCs is recommended.
- **In general, right hepatectomy is considered for type IIIa and type IV** lesions with predominant right side involvement, while left hepatectomy is preferred for type IIIb and type IV with predominant left side involvement.
- **Caudate lobectomy** The rationale behind caudate lobe resection is that its duct drains near the hepatic confluence, which increases the risk of involvement by tumor, and its routine resection improves the rate of R0 resection.
- **Caudate lobe resection should be routinely employed in patients with HC.**

Types of Hepatic Resection

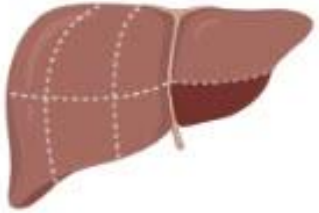
● Resection area



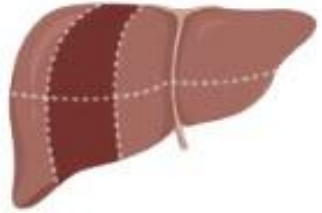
Liver anatomy
Hepatic sections



Wedge resection



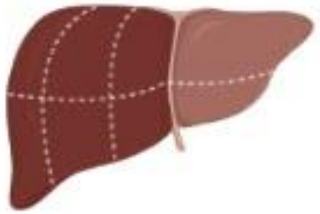
Segmentectomy



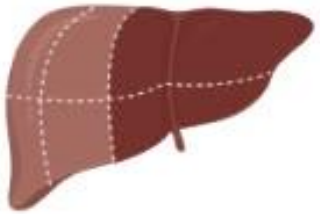
Right anterior sectionectomy



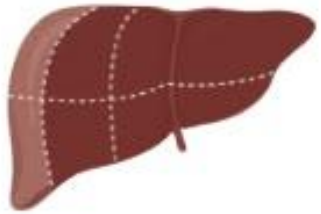
Right hepatectomy



Right extended hemihepatectomy



Left hepatectomy



Left extended hemihepatectomy

Determining resectability

iCCA staging uses TNM; tumour size, multifocality/bilaterality and vascular invasion are major prognostic variables.

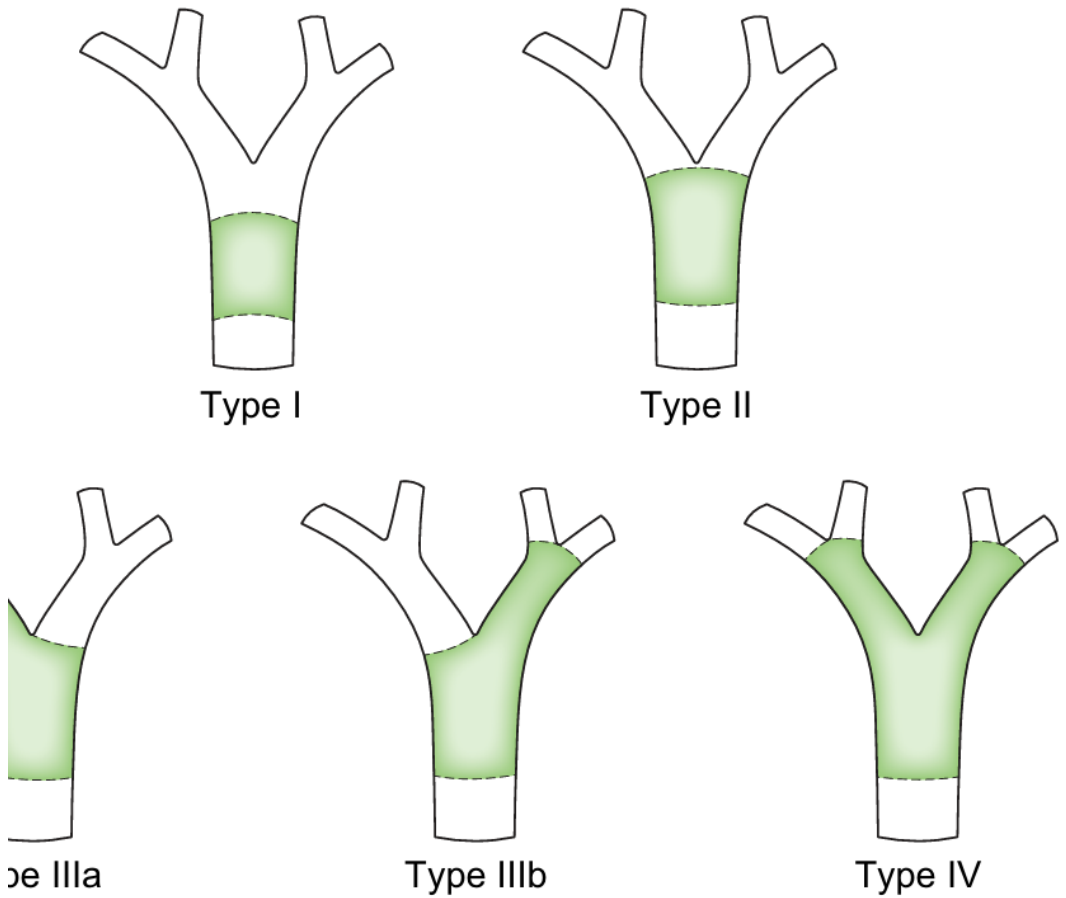
AJCC/UICC 8th edition: 5 cm separates T1a from T1b.

For pCCA, Bismuth–Corlette (BC) classification describes longitudinal extension relative to the common hepatic duct bifurcation.

BC type 1: distal to CHD; type 2: includes CHD; type 3a: right hepatic duct; type 3b: left hepatic duct; type 4: bilateral/multifocal ductal extension.

BC classification is anatomically useful but limited for predicting resectability and prognosis.

Bismuth-Corlette classification



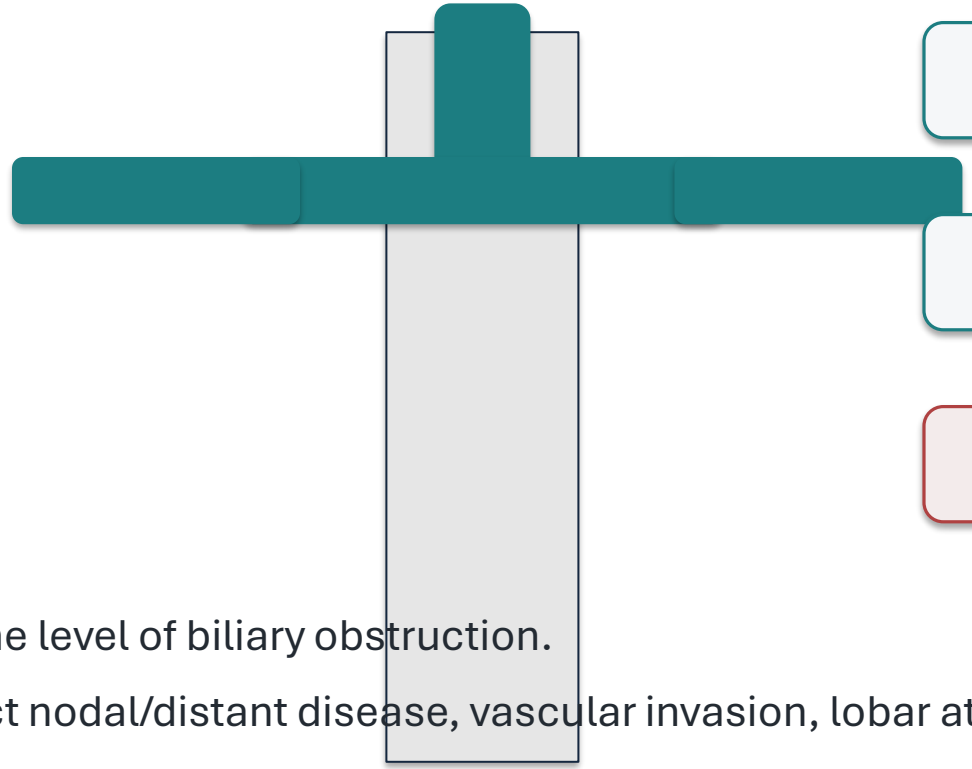
AJCC T classification, 8th edition	
Tis	Carcinoma *in situ*
T1	Confined to the bile duct
T2a	Invasion beyond the wall of the bile duct to surrounding adipose tissue
T2b	Invasion of adjacent hepatic parenchyma
T3	Invasion of unilateral PV or HA
T4	Invasion of the main bilateral PV/HA, or Bismuth type III with contralateral PV/HA involvement

Blumgart system	
T1	Bismuth type I to III without PV invasion or hepatic lobe atrophy
T2	Bismuth type I to III with ipsilateral PV invasion or/and hepatic lobe atrophy
T3	Bismuth IV, or Bismuth III with contralateral PV invasion or/and hepatic lobe atrophy or MPV or bilateral PV invasion

Perihilar disease: Bismuth is a map, not the whole decision

Type I

Type II



Type IIIa → right

Type IIIb → left

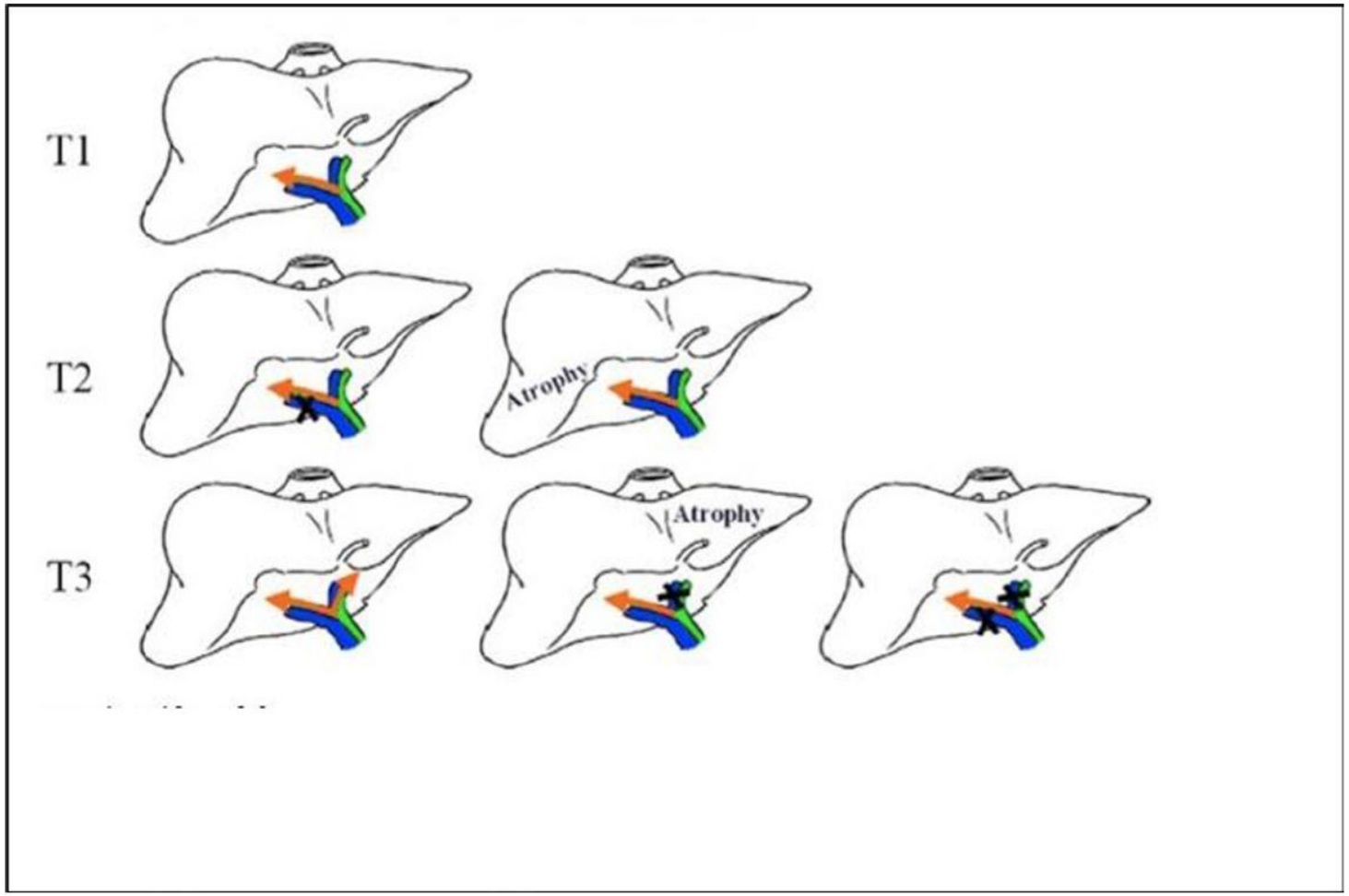
Type IV → bilateral ducts

Bismuth–Corlette classifies the level of biliary obstruction.

It does NOT adequately predict nodal/distant disease, vascular invasion, lobar atrophy or survival.

Modern planning therefore integrates ductal anatomy + portal/hepatic arterial anatomy + atrophy + metastases.

Schematic Representation of the Memorial Sloan- Kettering Cancer Centre classification system.



What makes pCCA unresectable?

Vascular

Portal vein or hepatic artery involvement on the future-remnant side without reconstructive options.

Biliary / local

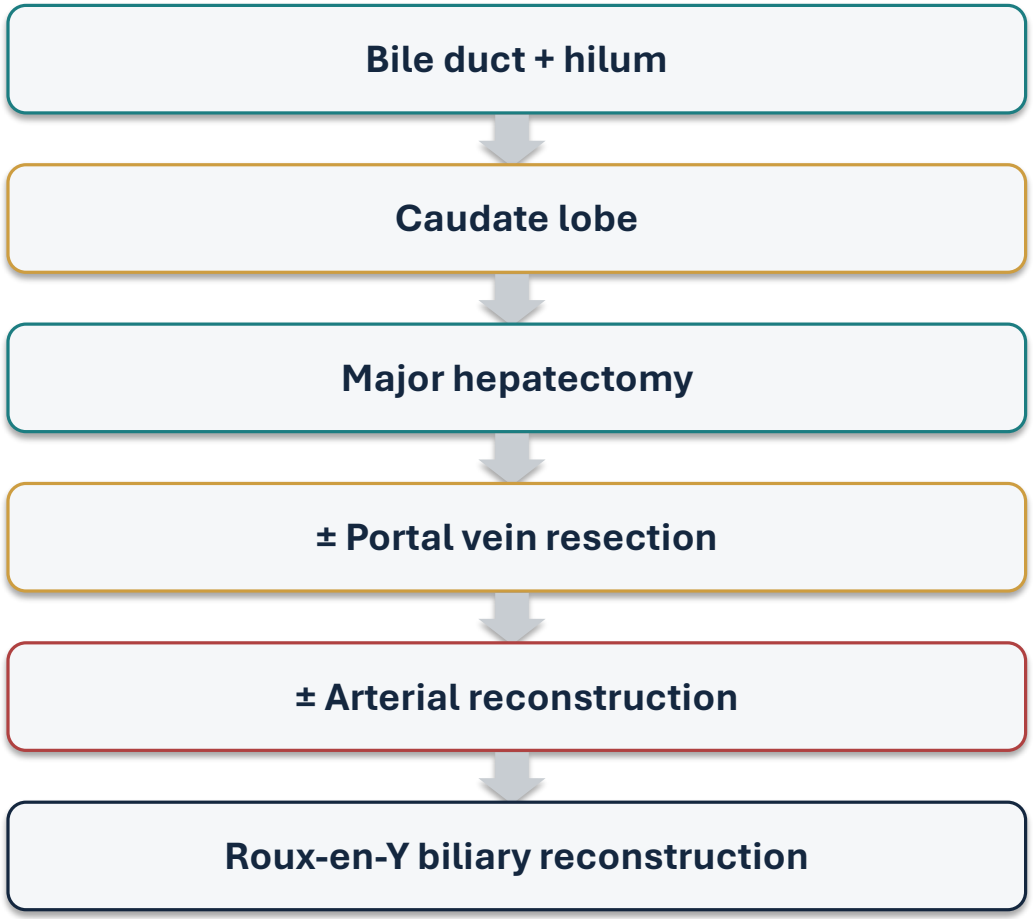
Extensive bilateral proximal infiltration into secondary biliary radicles and/or massive tumour extension into liver parenchyma.

Metastatic / patient factors

Distant metastases, extensive nodal disease beyond the hepatoduodenal ligament, or major comorbidity may preclude curative surgery.

The operation for perihilar cholangiocarcinoma

Think “en-bloc oncologic resection,” not local bile-duct excision



Right hepatectomy is commonly used for IIIa / right-dominant IV; left hepatectomy for IIIb / left-dominant IV.

Caudate resection is routinely recommended in the supplied review; omission increases the risk of R1 resection.

Portal vein involvement is no longer an automatic contraindication in experienced centers.

Arterial resection/reconstruction carries substantially greater risk and should be highly selective.

Predicting post-hepatectomy liver failure (PHLF)

PHLF may occur in up to 39.6% after major hepatectomy.

Assessment combines biochemical liver function, ICG testing and CT volumetry.

Other tools discussed include gadoxetic-acid enhanced MRI, which may add functional information beyond volume.

Clinical message

Adequate FLR is not simply a volume problem: combine morphology, perfusion, venous drainage and functional assessment.

Risk factors for PHLF

Patient-related

Advanced age • male sex • diabetes mellitus • metabolic disorders • malnutrition • renal insufficiency • hyperbilirubinaemia • thrombocytopenia

Surgery-related

Blood loss >1200 mL • transfusion • operative time >240 min • extended resection >50% • vena cava/vascular resection • duration of Pringle manoeuvre

FLR is often the real limiting factor

NORMAL LIVER	CHEMOTHERAPY-EXPOSED	CIRRHOSIS
FLR ≥20%	**~30% or more**	**>40%**

The exact threshold is not a single number: liver quality, prior chemotherapy and function matter.

PHLF is a dominant cause of death after major hepatectomy.

Use volumetry plus functional assessment when the anatomy is borderline.

If FLR is inadequate, augment before resection rather than accepting a small-for-size liver.

How to enlarge the future liver remnant

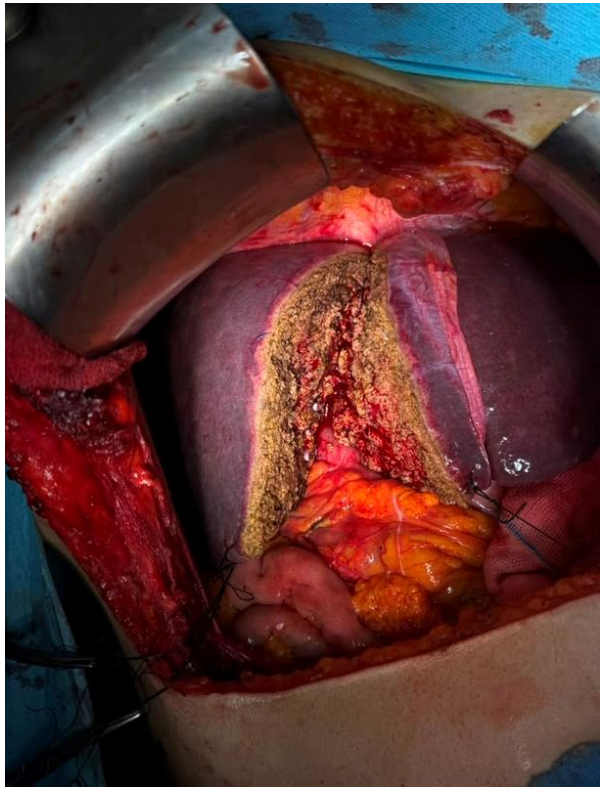
Strategy	Speed	Main advantage	Main concern
PVE	3–6 weeks	Established, safe, widely available	Tumor progression during waiting
LVD	Faster than PVE	More rapid / greater hypertrophy	Availability & expertise
ALPPS	Very rapid	Can rescue very small FLR	Higher morbidity; highly selective

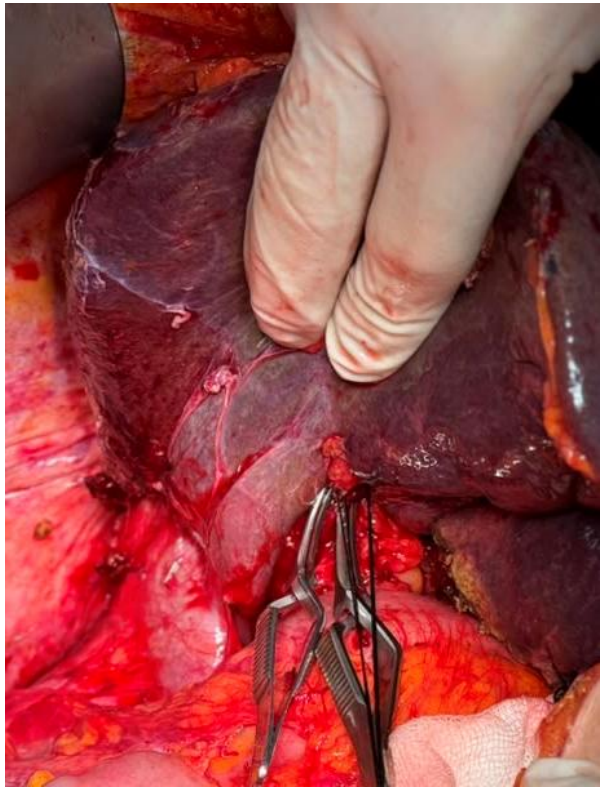
Practical hierarchy from the reviews: PVE first → consider LVD when faster hypertrophy is valuable → reserve ALPPS for selected rescue situations.

ASSOCIATING LIVER PARTITION AND PORTAL VEIN LIGATION WITH STAGED HEPATECTOMY

- **partial ALPPS** , preserving the artery to segment IV (prevent segment IV necrosis), minimizing the skeletonization of the hilar structures, and abandoning the plastic bag that was used to wrap the transected liver.
- **a) Central ALPPS**: Here, segments IV, V, and VIII are preserved. A left lateral sectionectomy is performed in stage I, along with ligation of the right posterior portal vein, and an in situ split along the right posterior portal fissure.
- **b) No touch ALPPS** (hybrid ALPPS): Here, the parenchymal transection is done via the anterior approach without dissection of the hilum, followed by PVE, while the second stage is performed 7"10 d later
- **c) Radiofrequency Assisted Liver Partition with Portal vein ligation (RALLP)**: This technique uses a series of radiofrequency coagulations along the proposed line of transaction to occlude the portal vein flow to segment IV.
- **d) Laparoscopic microwave ablation with portal vein ablation for staged hepatectomy (LAPS):** This is This is identical to RALLP, except that it uses microwave energy, rather than radiofrequency energy

ALPPS






iCCA: what makes an R0 resection worthwhile?

R0 STATUS	BIOLOGY	FLR
Margin ≥5–10 mm when feasible	Nodes • multifocality • vascular invasion • subtype	Do not trade liver failure for an extra few millimeters

Frozen section and margin assessment

Purpose

Frozen section assesses microscopic disease at the distal resection margin.

If invasive disease threatens the margin, further excision can be undertaken to achieve R0 resection.

Limitations

Sensitivity is reported at 60–70% in the source.

False-negative and false-positive results occur.

Preoperative biliary stenting may promote epithelial regeneration and contribute to false-negative interpretation.

Carcinoma in situ at the margin is described as not clearly worsening survival and may be treated as equivalent to a negative frozen section.

Vascular resection and lymphadenectomy

Vascular involvement

Portal vein invasion indicates locally advanced disease (T3/T4), yet selected patients undergoing portal vein resection may have survival comparable with major hepatectomy without portal vein resection.

Hepatic artery resection/reconstruction may be considered only in highly selected patients.

Lymph nodes

Adequate lymphadenectomy is essential for staging.

<5 nodes is associated with understaging and poorer observed survival.

The source cites acquisition of ~15 nodes as an optimal target for accurate staging/prognosis.

Lymphadenectomy: staging value is clearer than therapeutic value

iCCA

Regional lymphadenectomy is increasingly recommended for accurate staging.

The supplied 2025 review cites a minimum target of six nodes from the hepatoduodenal ligament/common hepatic artery region.

Therapeutic survival benefit remains unsettled after adjustment for stage and biology.

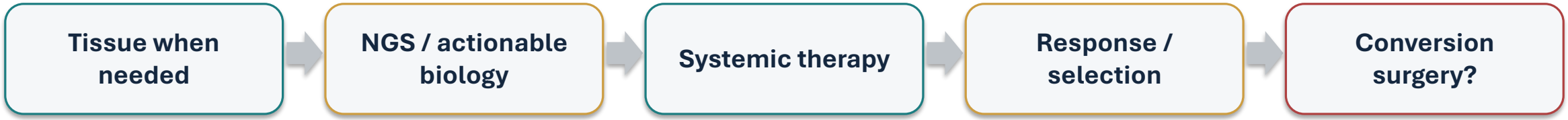
PERIHILAR

Regional nodal disease strongly affects prognosis.

Extended lymphadenectomy may improve staging and may benefit selected M0/R0 patients, but routine extended dissection remains controversial.

Distant nodal disease changes the curative calculus.

The oncologist is now part of the surgical decision — before the operation



Molecular alterations with direct therapeutic relevance include FGFR2 rearrangements and IDH1 mutations.

For borderline/unresectable disease, neoadjuvant/conversion therapy may select biology and occasionally enable resection.

The reviews support multidisciplinary planning rather than anatomy-only selection.

The surgical question becomes: “Is this tumor biologically controllable enough to justify a high-risk operation?”

Transplantation: not routine — but a real oncologic pathway in selected patien

PERIHILAR

The 2023 review supports LT for selected unresectable, non-metastatic hilar tumors.

Neoadjuvant chemoradiation/protocolized selection is central.

Organ scarcity means conventional R0 resection is preferred whenever safely achievable.

INTRAHEPATIC

The 2025 review describes a conditional, expanding role in early-stage or highly selected disease after neoadjuvant treatment.

Evidence remains much less mature than for the established hilar transplant pathway.

Locoregional treatment

Locoregional treatment

Surgery is preferred for resectable iCCA.

For lesions <3 cm, thermal ablation may be considered in selected high-risk surgical patients.

Larger lesions may be treated with transarterial approaches including TACE, Y-90 radioembolisation and hepatic arterial infusion chemotherapy.

transplantation

- iCCA remains a contraindication in most programmes worldwide.
-
- Selected pCCA patients—especially with chronic liver disease, tumour <3 cm and no extrahepatic disease—may achieve long-term disease-free survival with transplantation.

Distal CCA

- Surgical resection with microscopically negative margins, including radical en-bloc resection of surrounding structures and adequate lymphadenectomy, is the only potentially curative option for dCCA.

- Given the location of dCCA in the common bile duct between the ampulla of Vater and the junction of the cystic and common hepatic ducts, a pancreaticoduodenectomy is typically indicated.(Classic Versus Pylorus-preserving Pancreaticoduodenectomy

- Lymph Node Dissection:
- The AJCC has endorsed the retrieval of at least 12 nodes for adequate lymph node staging

What should the multidisciplinary tumor board decide?

RESECT NOW	Clear R0 pathway + adequate FLR + acceptable biology
AUGMENT	PVE / LVD when FLR is limiting
TREAT FIRST	Neoadjuvant / conversion systemic therapy
TRANSPLANT PATHWAY	Selected non-metastatic hilar disease or highly selected iCCA
PALLIATIVE / LOCoregional	When systemic or local control is the appropriate goal

Five take-home messages

1. R0 remains the surgical goal — but R0 must be balanced against FLR and liver function.

2. Perihilar cholangiocarcinoma often requires en-bloc major hepatectomy + caudate resection ± vascular reconstruction.

3. PVE remains the practical first-line FLR strategy; LVD is increasingly attractive; ALPPS is selective.

4. In iCCA, margin science, nodal staging and intraoperative ultrasound are as important as the type of hepatectomy.

5. Modern cholangiocarcinoma surgery is biology-guided and multidisciplinary: systemic therapy and molecular profiling can change who should be operated on.



Thank you for your attention