

Diagnosis and Management of Liver and Bile Duct Cancers



W. Thomas Purcell, MD

University of Colorado Cancer Center

April 26, 2014

CONFLICT OF INTEREST DISCLOSURE

- 1) Off-label use of chemotherapy will be discussed only in context of clinical research.**
- 2) No speakers bureaus; unpaid advisory boards only.**
- 3) I serve as PI of clinical trials (contracts are with University of Colorado) sponsored by Amgen and Bayer.**

Primary Sclerosing Cholangitis and Cancer

- Bile Duct Cancer (cholangiocarcinoma)
- Gallbladder Cancer (adenocarcinoma)
- Hepatocellular Carcinoma in patients with PSC and cirrhosis
- Colon Cancer (adenocarcinoma)



Cholangiocarcinomas

- Cholangiocarcinomas arise from the epithelial cells of the intrahepatic and extrahepatic bile ducts
- Most are locally advanced at presentation
- Account for 3% of all gastrointestinal malignancies
- Overall, rates of intrahepatic cholangiocarcinomas is increasing, but extrahepatic cholangiocarcinomas are declining



Risk Factors – All comers

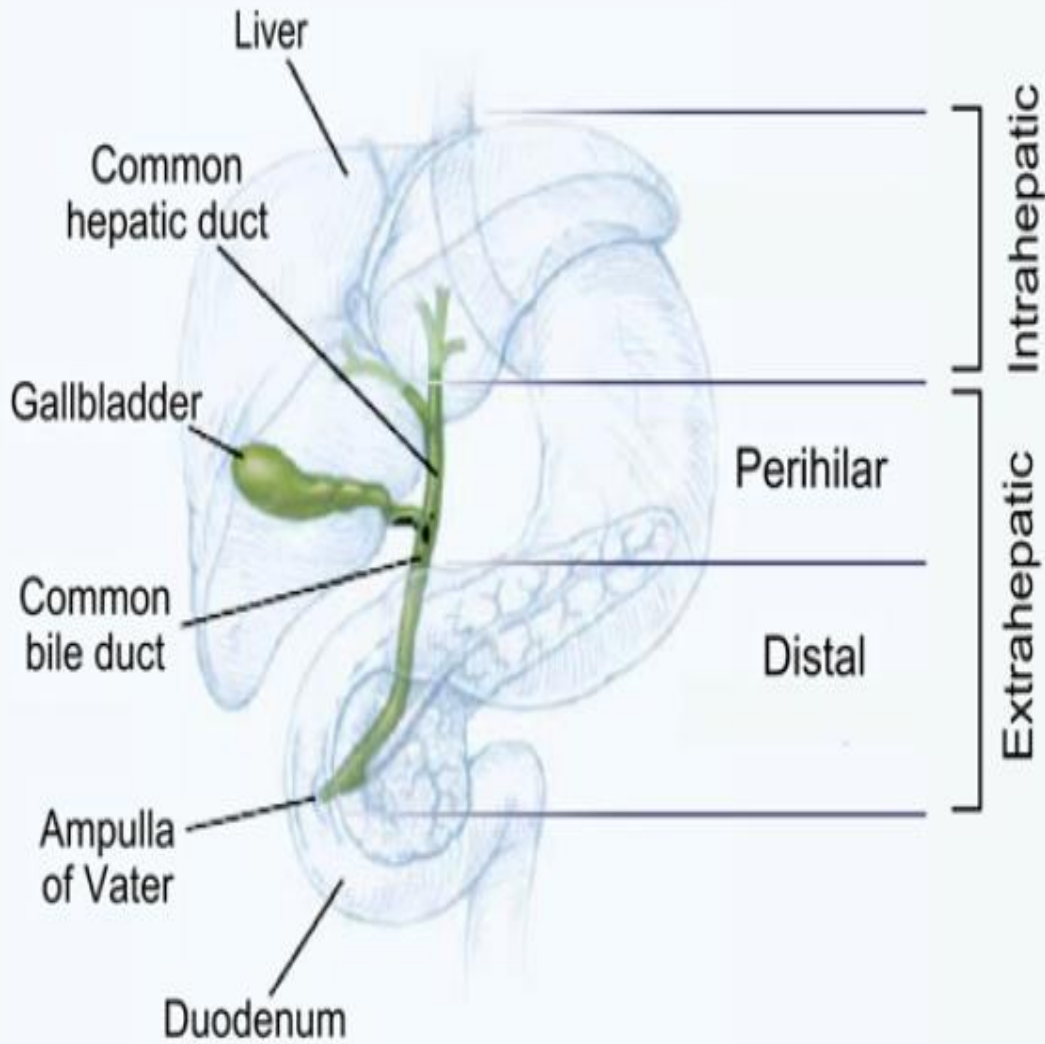
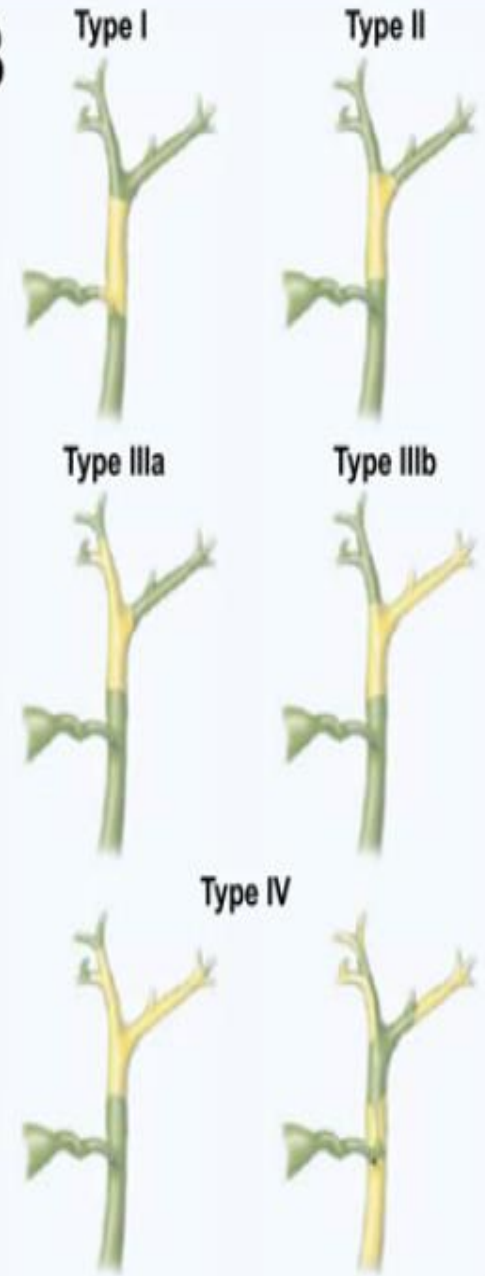
- Primary sclerosing cholangitis
 - Strongly associated with ulcerative colitis
 - Lifetime risk of 10%-15%
- Fibropolycystic liver disease
 - Congenital abnormalities of the biliary tree
- Parasitic infection
 - Liver flukes
- Cholelithiasis
- Lynch syndrome
- Chronic liver disease

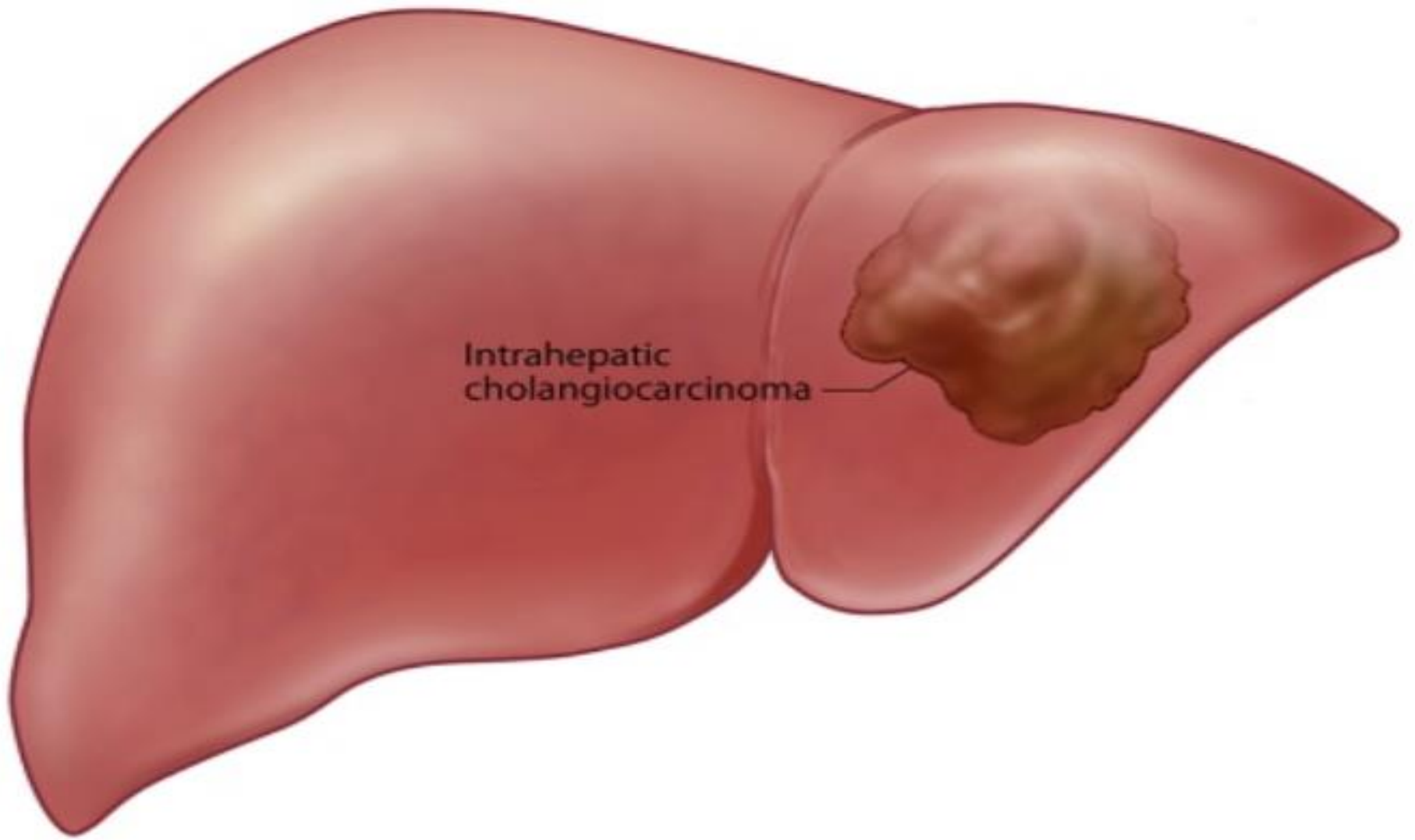


Cholangiocarcinoma and PSC

- Lifetime prevalence of 10-30%
- Annual risk 1.5% per year
- Difficult to diagnose

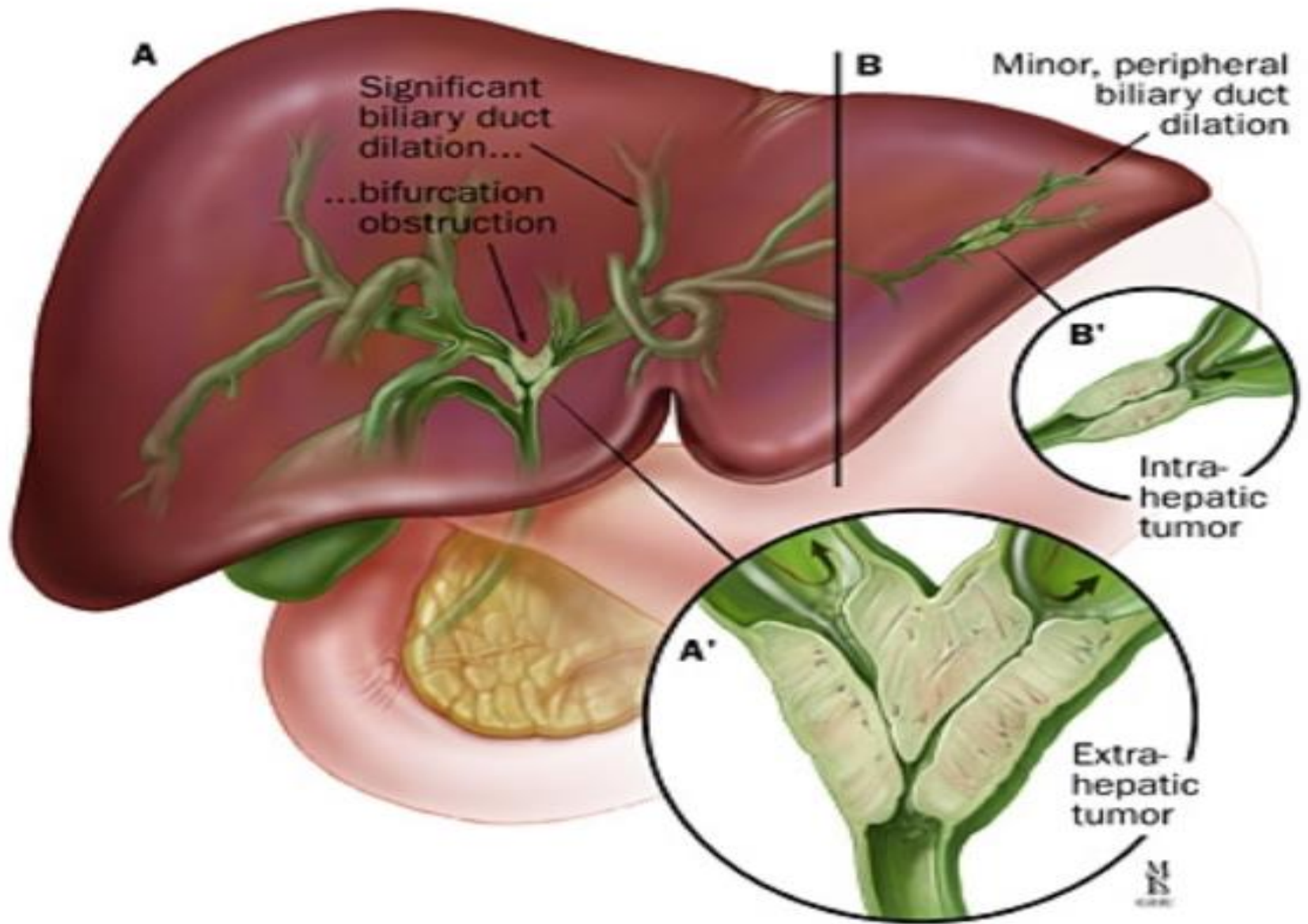


A**B**



Intrahepatic
cholangiocarcinoma

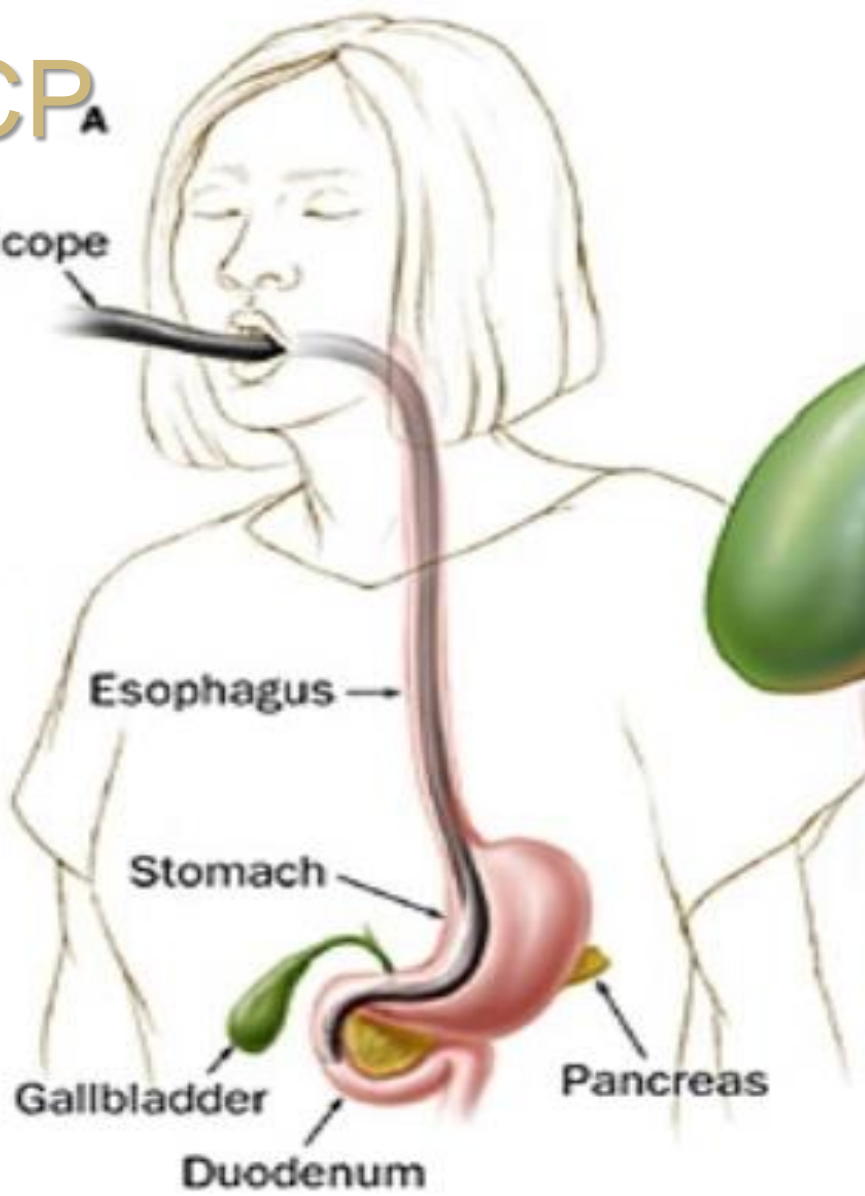
Intrahepatic Cholangiocarcinoma



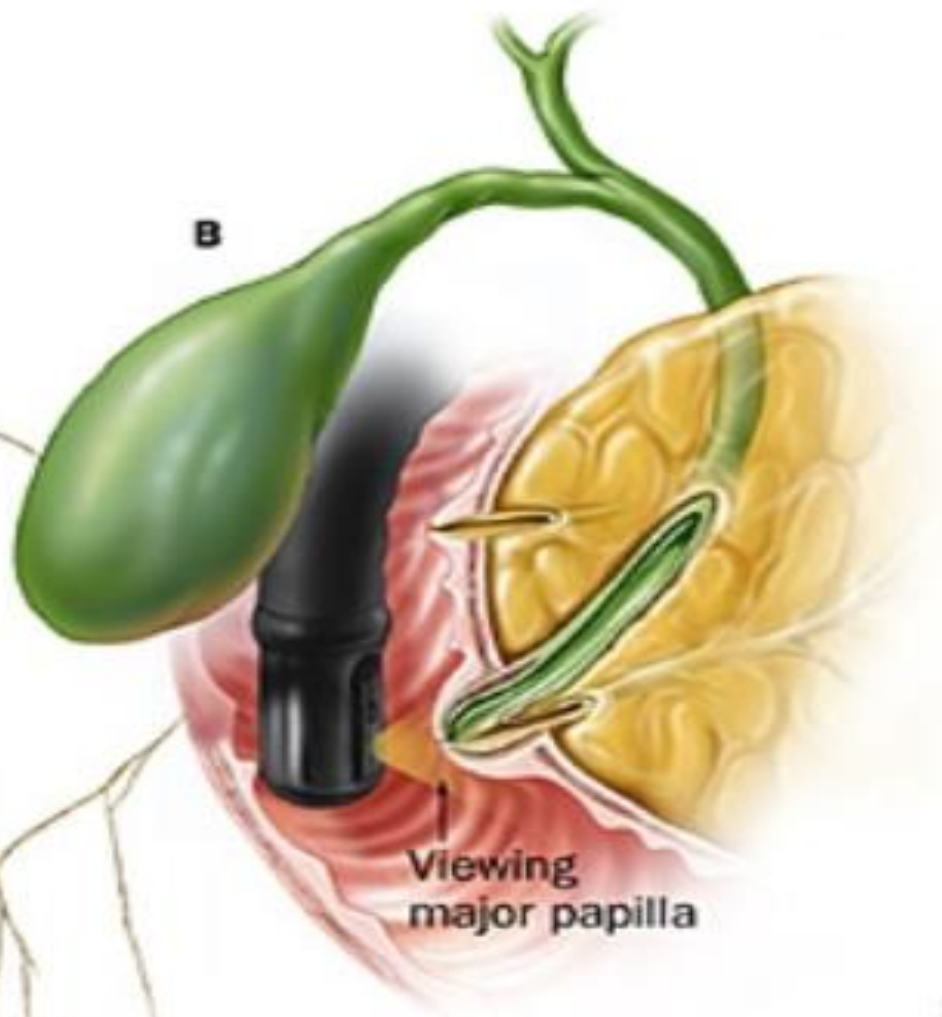
A, extrahepatic tumor; B, intrahepatic tumor resulting in a biliary duct dilation

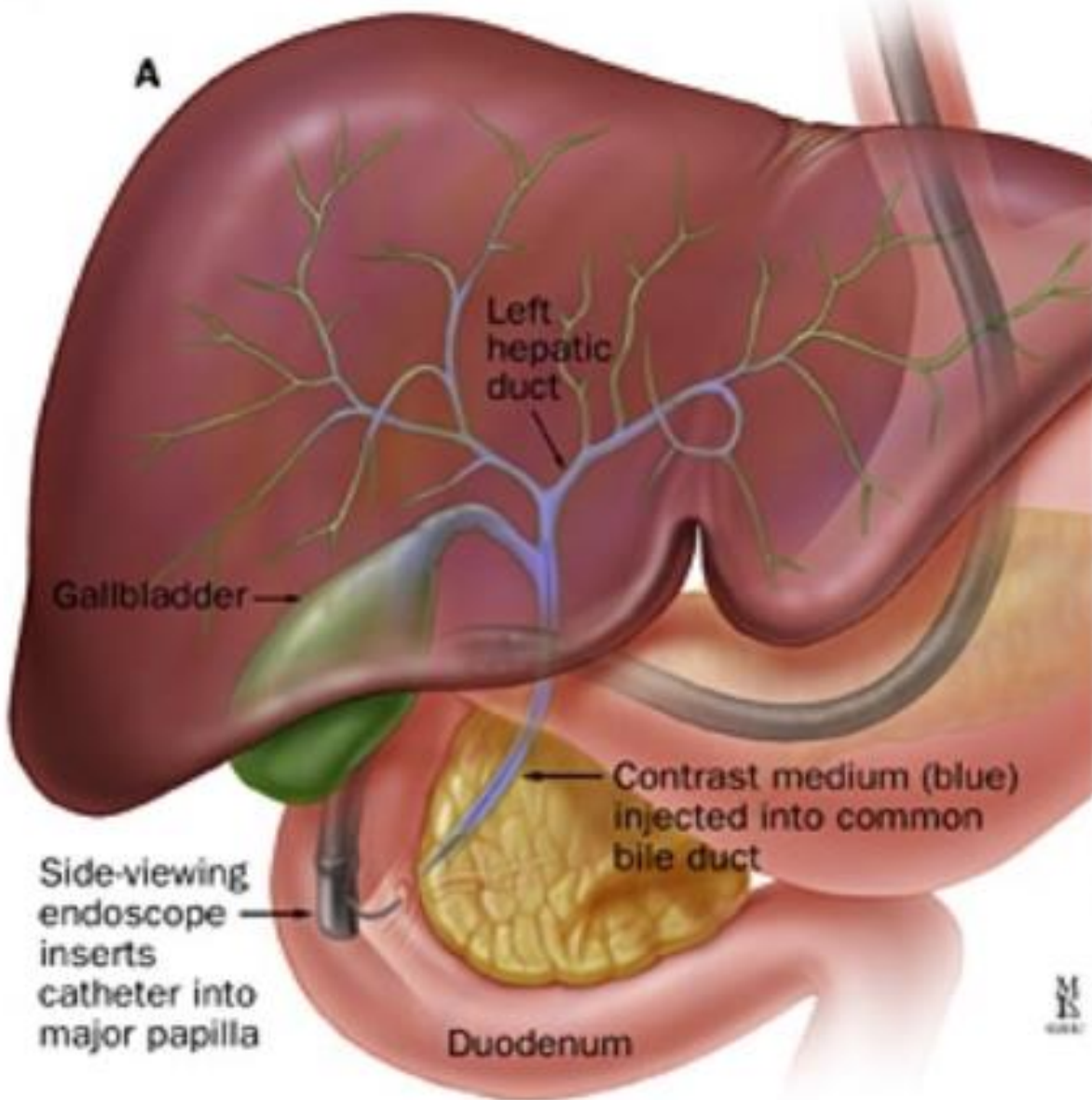
ERCP_A

Scope



B





A, B, Position of the endoscope in the duodenum during ERCP

Possible Symptoms at Diagnosis

- Painless jaundice
- Pruritus - itching (66%)
- Abdominal pain (30-50%)
- Weight loss (30-50%)
- Fever (up to 20%)



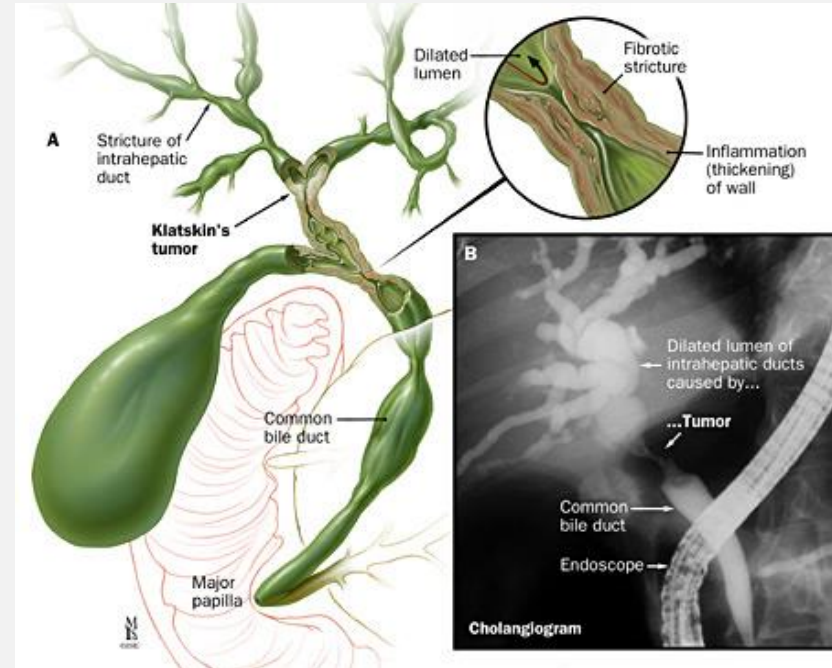
Laboratory Testing

- Elevations in total bilirubin
- Transaminitis (ALT/AST/Alkaline Phosphatase)
- CEA
- CA 19-9



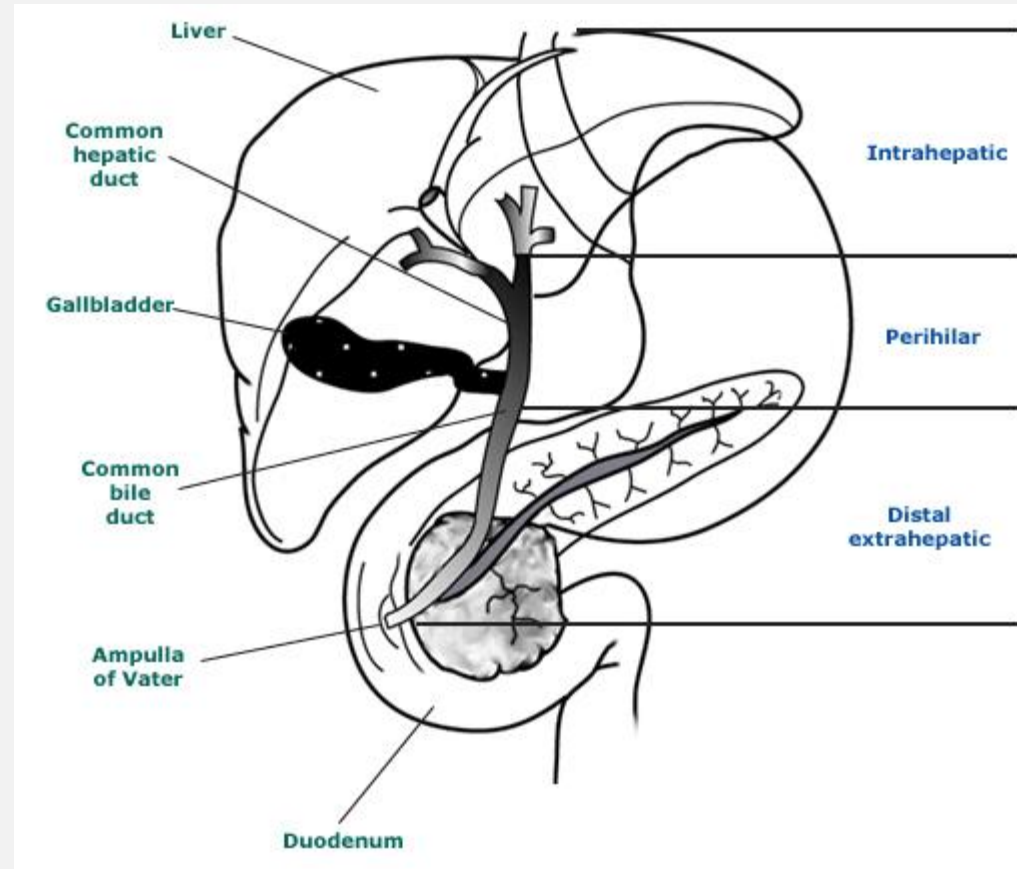
Radiographic evaluation

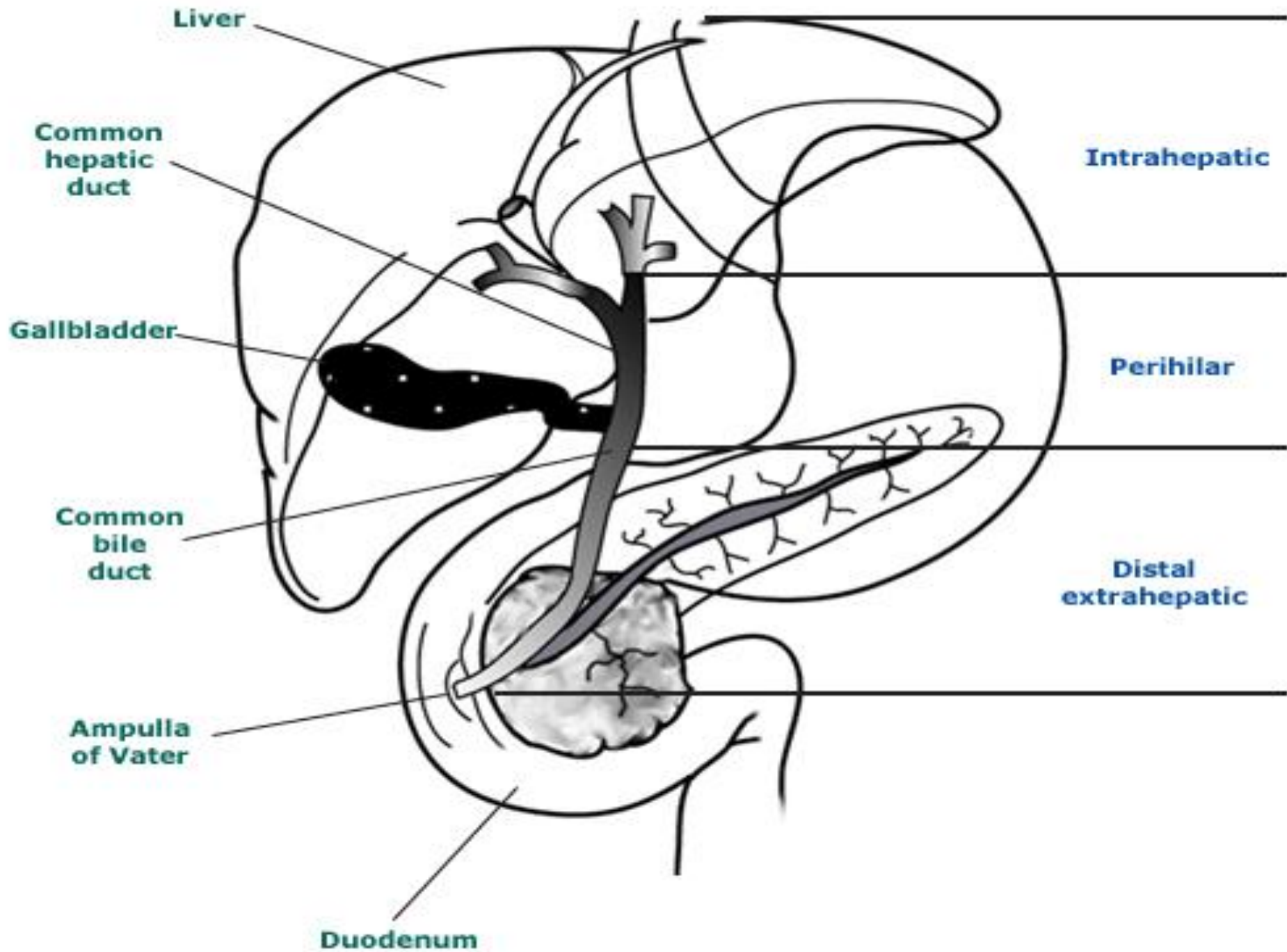
- Ultrasound
- CT Abdomen/Pelvis
- MRCP
- ERCP with brushing/biopsy
- Endoscopic ultrasound (EUS)



Anatomy

- Cholangiocarcinoma
 - Intrahepatic
 - Perihilar
 - Distal (extrahepatic)
 - Exclusive of the gallbladder or ampulla of Vater





Screening

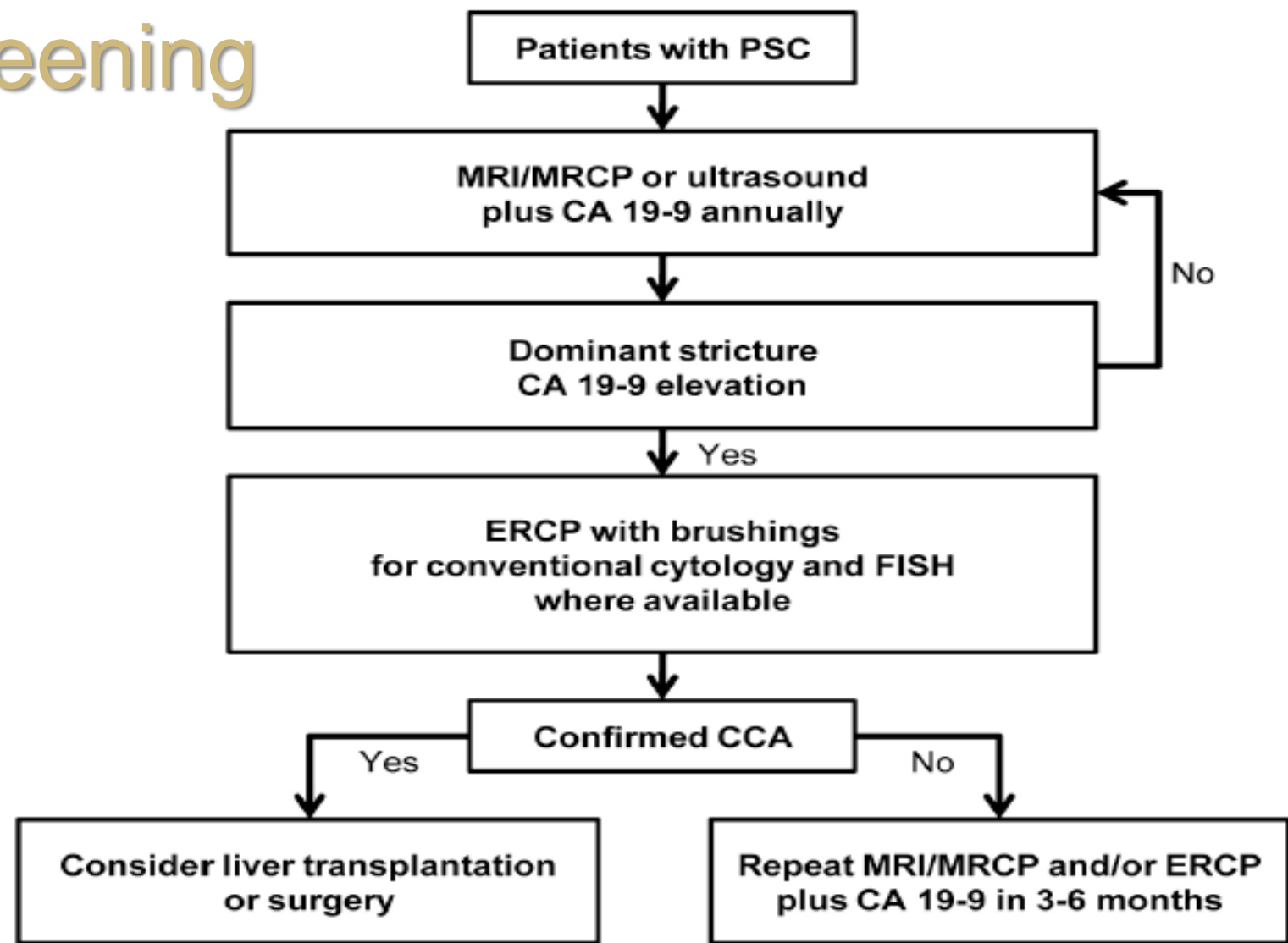


Fig. 1.

Recommendations for decision process for CCA surveillance in PSC. Abbreviations: CCA, cholangiocarcinoma; PSC, primary sclerosing cholangitis; MRI, magnetic resonance imaging; MRCP, magnetic resonance cholangiopancreatography; CA 19-9, carbohydrate antigen 19-9; ERCP, endoscopic retrograde cholangiopancreatography; FISH, fluorescence *in situ* hybridization.

Surgical Management

- Distal cholangiocarcinomas have higher resectability (**surgical removal**) rates while proximal tumors have the lowest
- Criteria for resectability
 - Absence of retropancreatic and paraceliac nodal metastases or liver metastases
 - Absence of invasion of the portal vein or main hepatic artery
 - Absence of extrahepatic adjacent organ invasion
 - Absence of disseminated disease



Surgical Treatment

- Intrahepatic cholangiocarcinoma
 - Usually treated by hepatic resection
 - *Consider liver transplantation if concomitant cirrhosis*
- Perihilar cholangiocarcinoma
 - Bile duct resection with hepatic resection
 - Chemoradiation followed by liver transplantation
- Distal cholangiocarcinoma
 - Usually treated with pancreaticoduodenectomy (Whipple procedure)
 - 5-year survival rates 23-50%



Prognostic Factors

- 5-year survival rates are 38% for lymph node-negative disease and $< 10\%$ for lymph node-positive disease
- 5-year rates are 19-47% for negative margins and 0-12% for positive margins



Locally-Advanced (unresectable) Cholangiocarcinomas

- Between 50 and 90% of patients with cholangiocarcinoma present with unresectable disease
- No role for tumor debulking
- Most patients receive 5-FU-based chemoradiotherapy
- Local palliation
 - TACE
 - Radioembolization
 - Radiofrequency ablation



Liver Transplantation

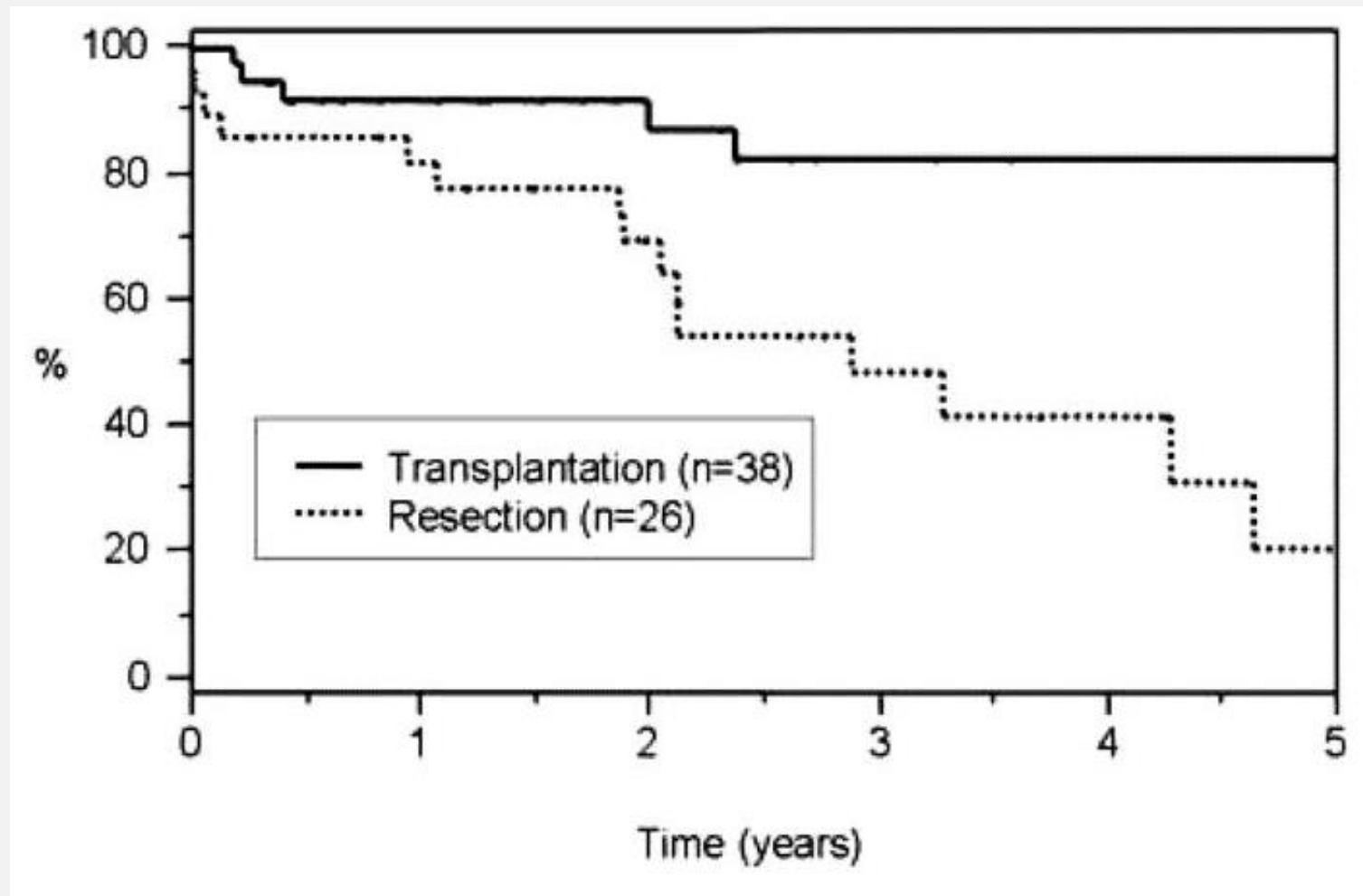
- Retrospective review of 71 patients with unresectable cholangiocarcinoma
 - No nodal involvement (stage I or II confirmed intraoperatively)
- Diagnostic criteria
 - Positive biopsy or cytology
 - CA 19-9 > 100 ng/mL
 - Positive FISH (~25-50% sensitivity and 67-88% specificity)
 - *Polysomy, tetrasomy, and trisomy of chromosome 7 or 3*
- Received neoadjuvant therapy with 5-FU and XRT
 - 5-FU 500mg/m² daily bolus for first 3 days of radiation
 - External beam radiotherapy 4500cGy in 30 fractions
 - 5-FU continued at same dose with an ambulatory infusion pump
 - Some patients received capecitabine 2000mg/m²/day in 2 doses



Liver Transplantation

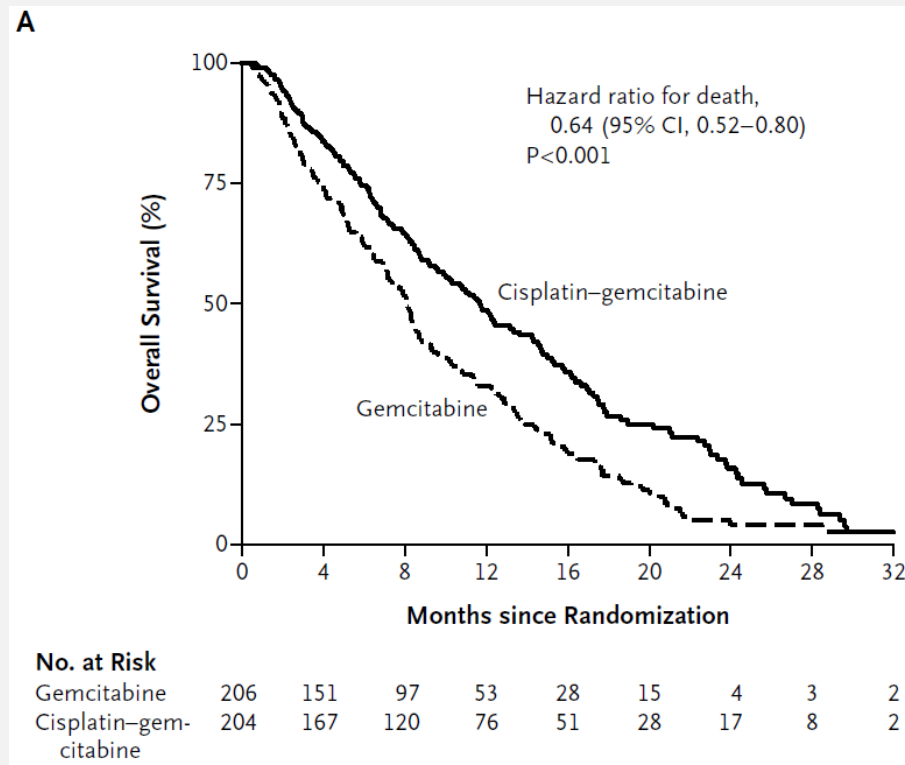
- 61 patients underwent operative staging
- 14 (23%) had findings precluding transplantation
- 38 patients underwent transplantation
 - 16 of 38 livers did not reveal any residual tumor
- Survival for 38 patients that underwent liver transplant was 82% at 5 years

Survival Rates After Transplant



Metastatic Cholangiocarcinomas

- Systemic chemotherapy for advanced cholangiocarcinomas
 - Gemcitabine plus cisplatin



Gallbladder Cancer

- Uncommon, but highly fatal malignancy
 - Fewer than 5000 new cases diagnosed each year in the United States
- Majority are found incidentally in patients undergoing exploration for cholelithiasis
- Poor prognosis thought to be related to advanced stage at diagnosis



Clinical Presentation

- Patients with early invasive GBC are often asymptomatic
- The most common complaint is pain
- Anorexia
- Nausea/Vomiting
- Obstructive Jaundice

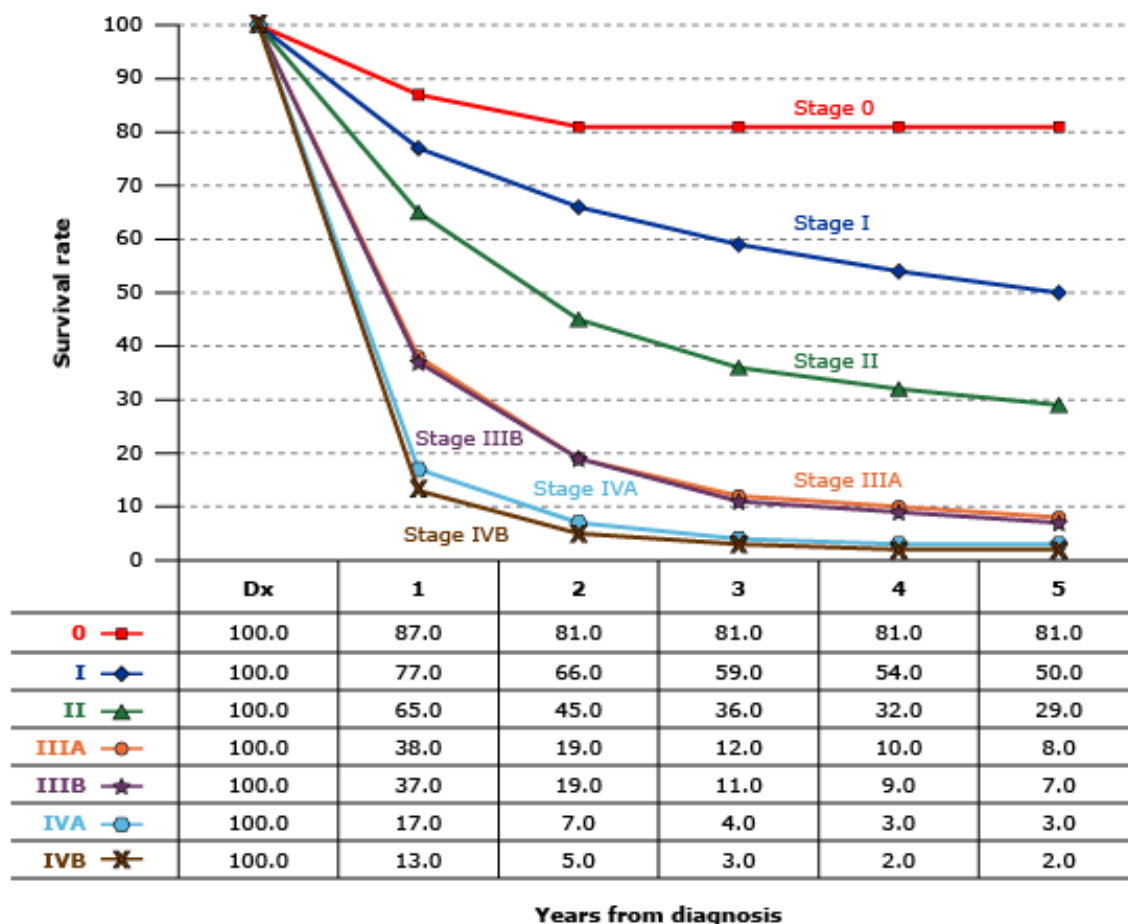


Diagnostic Evaluation

- Ultrasound
- Endoscopic Ultrasound (EUS)
 - More accurate
- CT/MRI
- Laboratory Studies
 - CA19-9 and CEA
 - Lack specificity and sensitivity



Observed survival rates for 10,705 gallbladder cancers



Data from the National Cancer Data Base (Commission on Cancer of the American College of Surgeons and the American Cancer Society) diagnosed in years 1989-1996.

Used with the permission of the American Joint Committee on Cancer (AJCC), Chicago, Illinois. The original source for this material is the AJCC Cancer Staging Manual, Seventh Edition (2010) published by Springer New York, Inc.

Surgical Treatment

- Surgery is the only potentially curative therapy
- Contraindications
 - Liver or peritoneal metastases
 - Ascites
 - Extensive involvement of the hepatoduodenal ligament
 - Nodal spread beyond the hepatoduodenal ligament
 - Encasement or occlusion of major vessels
- Five-year survival rates are 5-12 percent
- Risk of distant spread increases as T stage increases



Screening

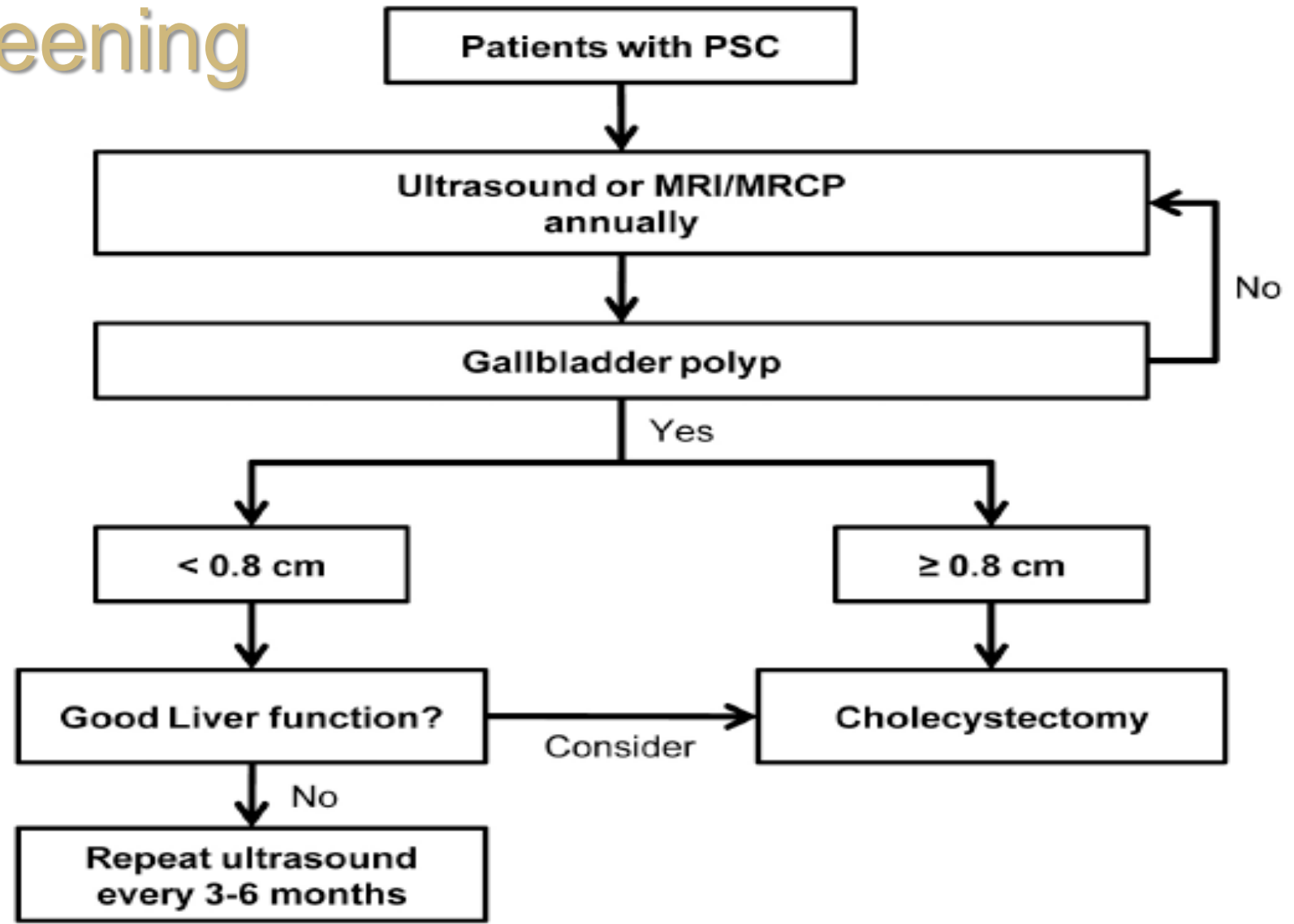


Fig. 2. Recommendations for decision process for GBC surveillance in PSC. Abbreviations: GBC, gallbladder cancer; PSC, primary sclerosing cholangitis; MRI, magnetic resonance imaging; MRCP, magnetic resonance cholangiopancreatography.

PSC / IBD and Colon Cancer

- 25% PSC develop cancer or dysplasia c/w 5.6% with UC alone
- Cancers associated with PSC tend to be more proximal (closer to cecum), more advanced at diagnosis and more likely to be fatal
- Need aggressive colonoscopic surveillance



Screening

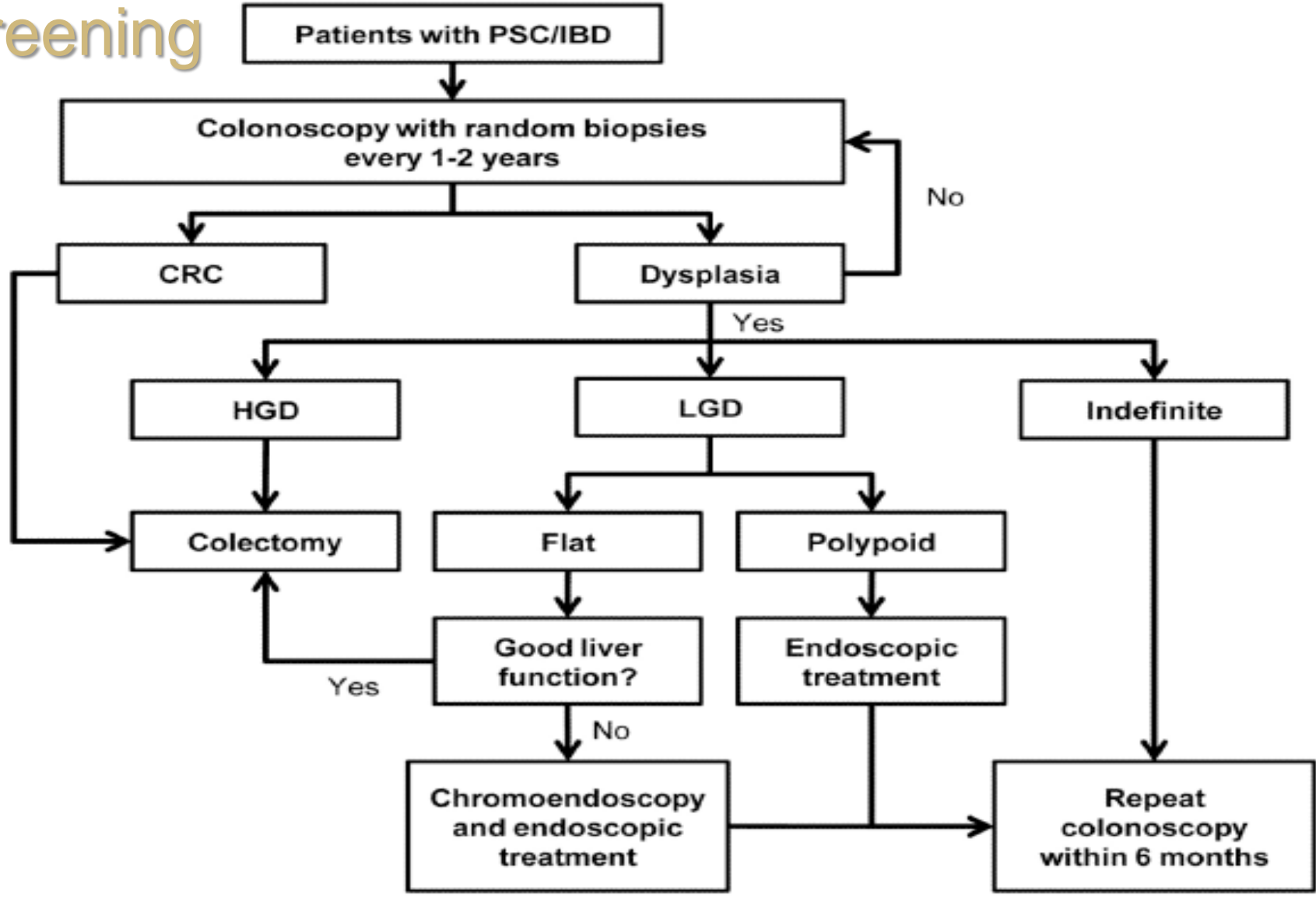


Fig. 3. Recommendations for decision process for CRC surveillance in PSC. Abbreviations: CRC, colorectal cancer; PSC, primary sclerosing cholangitis; IBD, inflammatory bowel disease; HGD, high-grade dysplasia; LGD, low-grade dysplasia.

Questions

