Cholangiocarcinoma

Lowe et al. “Epidemiology, pathogenesis, and classification of cholangiocarcinoma.” *UpToDate* v11.2.

**Key Points:**
- Incidence is associated with inflammatory risk factors.
- Intrahepatic cholangiocellular carcinoma presents differently from ductal cholangiocarcinoma, lacking obstructive symptoms / signs and mimicking hepatic metastases
- Diagnosis relies on combination of clinical scenario, imaging, tumor markers, and pathology, given poor sensitivities and specificities of diagnostic tests.
- Surgery is the only modality with mortality benefit; stenting offers palliation.

**Epidemiology**
- U.S.: 8 per million, peak age 50-70
  - Ductal: 2/3 (e.g., Klatskin tumors)
  - Intrahepatic cholangiocellular: 1/3?
    - Misdiagnosed as metastatic adenocarcinomas
    - Associated with hepatitis C in Japan
- Risk factors:
  - Primary sclerosing cholangitis (PSC): 1.5% per year, peak age 30-50, comprises 30% of new dx cancers,
  - *Clonorchis sinensis* and *Opisthorchis viverrini*
  - Caroli’s disease (7%)
  - Congenital choledochal cysts (up to 14%)
  - Chronic intrahepatic lithiasis (2-10%): not cholelithiasis
- Mechanisms: iNOS, interleukin 6, COX-2, c-erB-2 tyrosine kinase, p53, hTERT (inflammation)

**Clinical Presentation and Diagnosis**
- Ductal:
  - Obstruction: jaundice (90%), pruritus (66%), pale stools, dark urine
  - Abdominal pain (30-50%), weight loss (30-50%), fever (20%), cholangitis
  - Courvoisier’s sign (palpable gallbladder): rare
- Intrahepatic: abdominal pain, mass, anorexia, weight loss, night sweats, malaise, asymptomatic
  - Jaundice is rare
- Imaging
  - Ductal dilatation without stone: false negatives in PSC or cirrhosis
  - Atrophy-hypertrophy complex
  - MRCP
  - PET [18F]2-deoxy-D-glucose: false-positives
- Laboratory tests (most studied in patients with PSC)
  - Serum CA 19-9 ( > 100 U/mL): when cholangitis or cholestasis, diagnosis of malignancy requires higher cut-off for specificity
  - CEA: not sensitive or specific; possible role for combined index (CA 19-9 + CEAx40)
- ERCP / percutaneous transhepatic cholangiogram (PTC): diagnostic and therapeutic
  - Biopsy and brushings: 30-70% sensitive, 90% specific
- Patients with PSC: serial CA 19-9, PET scan (MRI not useful)

**Treatment**
- Determined by:
  - Local extent: distal > proximal
  - Vascular involvement
Metastases
- Investigated by MRCP, endoscopic U/S (15-20% metastatic lymph nodes), laparoscopy

**Surgery:**
- Complete resection: 40-60% 3-year survival
- Only for curative intent
- 10% operative mortality, mostly from infection – increased with stenting
- Possible benefit in post-operative hepatic function if bilirubin >3-10
- PSC: risk of hepatic decompensation
- Liver transplantation: role uncertain

**Palliative: survival <18 months**
- **Stenting**
  - Only if not operative candidates
  - Metallic stents (longer) vs. plastic (adjustable)
- Chemotherapy / radiation: partial response rates with 5-FU and gemcitabine, but no survival benefit
- Photodynamic therapy: hematoporphyrin derivative -> laser during ERCP