**Epidemiology and Symptoms**

- At least 70-80% of patients with PSC have IBD.
- PSC-AIH overlap occurs in up to 5% of adults.

- Symptoms include:
  - Fatigue and pruritus (can occur in absence of biliary obstruction).
  - Anxiety/Depression
  - Abdominal and fever

**Diagnosis**

- Consider in all patients with ↑ ALP +/- GGT.
- Exclude secondary sclerosing cholangitis.
- Measure serum IgG4 to exclude IgG4-sclerosing cholangitis.
- Obtain MRI/MRCP with contrast enhancement.
  - Normal → consider liver biopsy to rule out small duct PSC.
  - Equivocal → consider repeating MRCP or liver biopsy.
- Avoid using ERCP for diagnosis.
- Do not perform liver biopsy for confirmation except if there is a concern of AIH/PSC overlap.
- Perform ileocolonoscopy with biopsies in patients with new diagnosis of PSC without concurrent IBD.

**Surveillance**

- MRI/MRCP every 3-5 years for small-duct PSC (to look for development of large duct disease).
- Annual MRI/MRCP +/- CA19-9 for cholangiocarcinoma and gallbladder carcinoma.
- Ultrasound every 6 months if have gallbladder polyps ≤ 8 mm.
- Cholecystectomy if have gallbladder polyps >8 mm.
- HCC surveillance only if PSC with cirrhosis.
- Colonoscopy every 1-2 years if PSC with IBD.

**Fibrosis Staging**

- Should be done at diagnosis of PSC and regularly during follow-up but optimal frequency is unclear.
- Transient elastography or MRE = preferred method for measuring liver stiffness.
- Do not recommend liver biopsy for fibrosis staging.
### Indications for ERCP:
- New or worsening pruritus
- Weight loss
- ↑ liver enzymes
- ↑ CA 19-9
- Recurrent bacterial cholangitis
- ↑ bile duct dilation

- Need prophylactic antibiotics during periprocedural period.
- Biliary balloon dilation +/- stenting up to discretion of the individual endoscopist.
- If plastic stent placed, usually remove within 4 weeks.
- Sample intraductal tissue for cytology and FISH for relevant strictures.

### Indications for transplant:
- PSC with cirrhosis
- Recurrent cholangitis
- Intractable pruritus
- Early-stage hepatobiliary malignancies

- If liver enzymes ↑ post transplant, consider recurrent PSC versus rejection or biliary complications

### Management
- Consider **ursodeoxycholic acid** (UDCA, 13-23 mg/kg/day) for treatment in patients with consistently elevated ALP or GGT.
- Can continue UDCA if there is a ↓ (ALP < 1.5 x ULN, 40% reduction of ALP) or normalization of ALP or improvement of symptoms with 12 months of treatment.
- **No role for oral vancomycin** given insufficient evidence.
- Treat PSC/AIH overlap per AIH guidelines.
- Screen for varices if the liver stiffness is >20 kPA by transient elastography or the platelet count is ≤ 150,000/mm³.
- Consider **bile acid sequestrants** for pruritus if no improvement with measures such as anti-histamines, heat avoidance, or emollients.
- **Alternative therapy for pruritus** include sertraline 100 mg daily, naltrexone titrated to a dose of 50-100 mg daily, and rifampin 150-300 mg twice daily.
- Annual serum measurements of Vit A, D, E, and K
- **DEXA scan** at diagnosis and every 2-3 years based on risk factors.
### Types of CCA

**Intrahepatic CCA (iCCA)**
- Arises proximal to second-order bile ducts within the hepatic parenchyma.

**Perihilar CCA (pCCA)**
- Arises between second-order bile ducts and the cystic duct insertion.

**Distal CCA (dCCA)**
- Arises in the common bile duct (CBD) below the cystic duct insertion.

### Risk factors for CCA

<table>
<thead>
<tr>
<th>Type</th>
<th>CA 19-9</th>
<th>Multiphasic CT and MRI</th>
<th>ERCP with biliary brushings</th>
<th>Biopsy</th>
</tr>
</thead>
<tbody>
<tr>
<td>iCCA</td>
<td>Not sufficient alone</td>
<td>Needed for assessing primary mass, vascular encasement</td>
<td>Requires ERCP</td>
<td>Requires biopsy for definitive diagnosis</td>
</tr>
<tr>
<td>pCCA</td>
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</tr>
<tr>
<td>dCCA</td>
<td>Not sufficient alone</td>
<td>Needed for assessing primary mass, vascular encasement</td>
<td>Requires ERCP</td>
<td>Requires biopsy for definitive diagnosis</td>
</tr>
</tbody>
</table>

### iCCA Work-Up
- CA 19-9 **not sufficient alone** for diagnosis. Levels > 1000 U/ml may allude to metastatic disease.
- **Multiphasic CT and MRI** are needed for assessing primary mass, detecting metastases, and staging disease.
- Requires **biopsy** for definitive diagnosis.

### iCCA Management

- Suggested treatment options for iCCA:
  - Resectable
  - Surgery
  - Adjuvant capcetibine
  - Consider referral to a liver transplant center

- Management of iCCA in the setting of metastasis or vascular encasement:
  - Single lesion ≤ 2 cm
  - Preserved liver function, ECOG ≤ 2
  - Systemic therapy: 1st line gemcitabine/platinum
  - Second line: FOLFOX
  - Clinical Trials: next generation sequencing, targeted therapy, immunotherapy
  - Decompensated liver function and/or ECOG > 2
  - Best supportive care

- Insufficient data to recommend liver directed therapies for iCCA.
AASLD Practice Guidance on Primary Sclerosing Cholangitis (PSC) and Cholangiocarcinoma (CCA) – Part II on CCA

Infographics Creator – Cindy Ye

Bowlus, Christopher L.1; Arrivé, Lionel2; Bergquist, Annika1; Deneau, Mark4; Forman, Lisa1; Ilyas, Sumera I.6; Lunsford, Keri E.7; Martinez, Mercedes8; Sapisochin, Gonzalo9; Shroff, Rachna10; Tabibian, James H.11; Assis, David N.13. AASLD practice guidance on primary sclerosing cholangitis and cholangiocarcinoma. Hepatology ():p n/a, October 20, 2022. | DOI: 10.1002/hep.32771

**pCCA Management**

- Resectable
  - Surgery
  - Adjuvant capcitabine
- Unresectable
  - Candidate for transplant • Single lesion with radial diameter ≤ 3 cm • No metastatic disease
  - Single lesion > 1 cm and/or presence of intra- or extrahepatic metastasis
  - Liver transplantation following neoadjuvant therapy
  - Preserved liver function, ECOG ≤ 2
  - Decompensated liver function and/or ECOG > 2
  - Systemic therapy • First line: gemcitabine/cisplatin • Second line: FOLF Ox • Clinical Trials: next generation sequencing, targeted therapy, immunotherapy
  - Best supportive care

**dCCA Management**

- Resectable
  - Pancreatoduodenectomy
  - Preserved liver function, ECOG ≤ 2
  - Adjunct capcitabine
- Unresectable
  - Decompensated liver function and/or ECOG > 2
  - Systemic therapy • First line: gemcitabine/cisplatin • Second line: FOLF Ox • Clinical Trials: next generation sequencing, targeted therapy, immunotherapy
  - Best supportive care

**dCCA Work-Up**

- **Multiphasic CT and MRI** are needed for assessing primary mass and vascular encasement.
- **Obtain CA 19-9** and consider IgG4 levels to exclude IgG4 sclerosing cholangiopathy.
- **Requires ERCP** with biliary brushings for cytology and FISH analysis and EUS with FNA for detailed examination of the extrahepatic bile duct and tissue acquisition. EUS-FNA has higher sensitivity of detection for dCCA than pCCA.

**Systemic Therapy**

- First line for advanced CCA.
- Gemcitabine/cisplatin is the first line treatment.
- FOLF Ox is the second line treatment.
- Consider referral to centers with expertise in hepatobiliary malignancies and clinical trials.