ACG Clinical Guideline: Chronic Pancreatitis
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The Emoroid Digest
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Definition

- A pathologic fibroinflammatory syndrome of the pancreas in individuals with genetic, environmental, and/or other risk factors who develop persistent pathologic responses to parenchymal injury or stress
- 60% of CP cases evolved from acute pancreatitis and recurrent acute pancreatitis (RAP), whereas about 10% of acute pancreatitis and 30% of RAP progress to CP

Etiology of CP

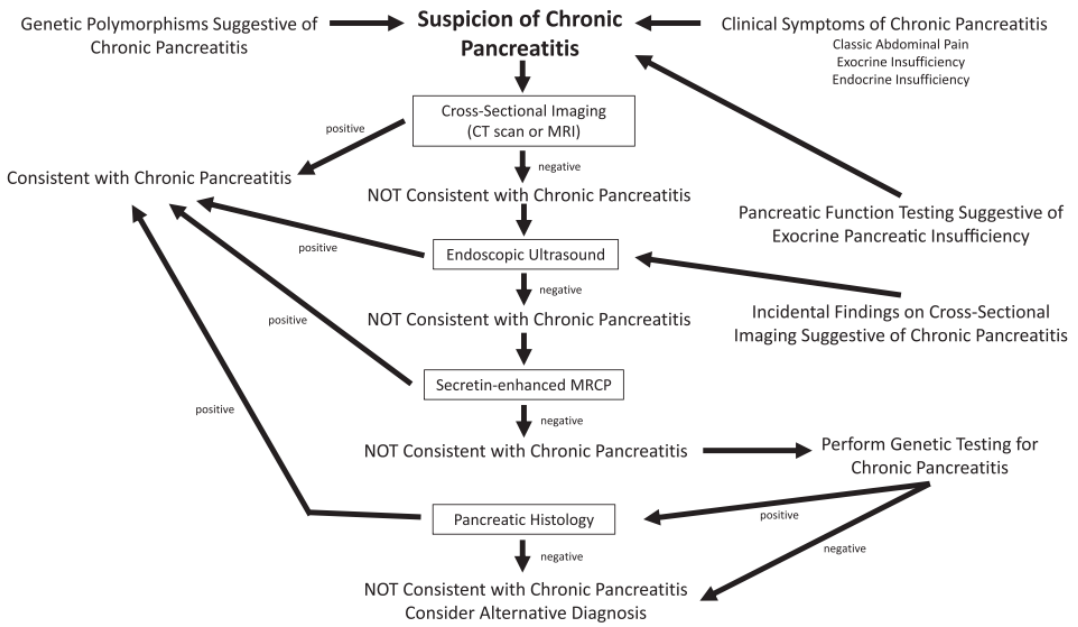
- Review all risk factors in patients with clinical evidence of CP and complete a thorough H&P
- ***TIGAR-O system:*** helps categorize an etiology to explain CP
  - T (Toxic-Metabolic)
  - I (Idiopathic)
  - G (Genetic)
  - A (Autoimmune)
  - R (Recurrent acute or severe pancreatitis)
  - O (Obstructive)

Diagnosis

- ***1st line:*** CT or MRI
- ***2nd line:*** EUS only if diagnosis is in question after cross-sectional imaging
- ***3rd line:*** secretin-enhanced MRCP if diagnosis in question after cross-sectional imaging or EUS
- ***4th line:*** histologic diagnosis with EUS-guided FNA (low sensitivity)

Clinical Manifestations

- Abdominal pain
- Fat-soluble vitamin deficiency -> malnutrition/osteoporosis
  - Periodic monitoring of fat-soluble vitamins and zinc
- Risk of pancreatic malignancy
  - No screening recs
- Endocrine insufficiency manifesting as DM (T3cDM from islet cell loss)
  - ↑ with duration of disease
  - BMI and smoking status may increase risk



Toxic-metabolic
Alcohol-related (susceptibility and/or progression)
3–4 drinks/d
5 or more drinks/d
Smoking (if yes, record pack-years)
Nonsmoker (<100 cigarettes in lifetime)
Past smoker
Current smoker
Other, NOS
Hypercalcemia—(ionized calcium levels >12.0 mg/dL or 3 mmol/L)
Hypertriglyceridemia
Hypertriglyceridemic risk—(fasting >300 mg/dL; nonfasting >500 mg/dL)
Hypertriglyceridemic acute pancreatitis, history of (>500 mg/dL in the first 72 hr)
Medications (name)
Toxins, other
CKD—(CKD stage 5—ESRD)
Other, NOS
Metabolic, other
Diabetes mellitus (with the date of diagnosis if available)
Other, NOS
Idiopathic
Early onset (<35 yr of age)
Late onset (>35 yr of age)
Genetic
Suspected; no or limited genotyping available
Autosomal dominant (Mendelian inheritance—single-gene syndrome)
PRSS1 mutations (hereditary pancreatitis)
Autosomal recessive (Mendelian inheritance—single-gene syndrome)
CFTR, 2 severe variants in trans (cystic fibrosis)
CFTR, <2 severe variants in trans (CFTR-RD)
SPINK1, 2 pathogenic variants in trans (SPINK1-associated familial pancreatitis)
Complex genetics—(non-Mendelian, complex genotypes +/– environment)
Modifier genes (list pathogenic genetic variants)
PRSS1-PRSS1 locus
CLDN2 locus
Others
Hypertriglyceridemia (list pathogenic genetic variants)
Other, NOS
AIP/steroid-responsive pancreatitis
AIP type 1—IgG4-related disease
AIP type 2
RAP and SAP
Acute pancreatitis (single episode, including date of event if available)
AP etiology—extrapancreatic (excluding alcoholic, HTG, hypercalcemia, and genetic)
Biliary pancreatitis
Post-ERCP
Traumatic
Undetermined or NOS
RAP (number of episodes, frequency, and dates of events if available)
Obstructive
Pancreas divisum
Ampullary stenosis
Main duct pancreatic stones
Widespread pancreatic calcifications
Main pancreatic duct strictures
Localized mass causing duct obstruction

Gardner, et al. ACG Clinical Guideline: Chronic Pancreatitis. Am J Gastroenterol 2020;115:322–339.

Direct and Indirect Pancreatic Function Tests

- Help diagnose exocrine pancreatic insufficiency (EPI) but role in diagnosing CP is adjunctive
- ***Nonhormonal***
  - *Fecal elastase:* universally available; limited use in mild disease, limited specificity in diarrhea
  - *Serum trypsinogen/trypsin:* easily obtainable, can quantify to track function over time; elevated with pancreatic pain and does not measure digestive tract enzymes
- ***Hormonal***
  - *CCK stimulation test:* direct acinar cell function/subtle EPI; cumbersome and not widely available
  - *Secretin stimulation test:* direct ductal cell function and ductal secretory ability; not widely available and prone to measurement error

Test	Advantages	Disadvantages
Hormonal tests of pancreatic function		
CCK stimulation test (acinar cell stimulation measuring trypsin and/or lipase)	Direct acinar cell function Detects subtle EPI	Cumbersome Not widely available Specialized laboratory testing required Patient discomfort with Dreiling tube placement 2–3 hr test
Secretin stimulation test (ductal cell stimulation measuring bicarbonate)	Direct ductal cell function Performed endoscopically Uses laboratory autoanalyzer 60 min test Measures ductal secretory ability	Not widely available Prone to measurement error Risk and cost of endoscopy
Nonhormonal tests of pancreatic function		
Fecal elastase-1	Universally available Easily obtainable Noninvasive	Moderate sensitivity Limited specificity in diarrhea Limited use in mild disease
^{13}C-mixed triglyceride test	Easily obtainable High sensitivity (90%)	Not universally available Long test duration—4–6 hr
Serum trypsinogen/trypsin	Universally available Easily obtainable Noninvasive Quantifiable for tracking function over time	Does not measure digestive tract enzymes Elevated with pancreatic pain

Suspicion of Chronic Pancreatitis

	Clinical Features	← PLUS → Risk (TIGAR-O)	Imaging	Serum markers	← PLUS → Biomarkers
a	Pancreatitis-like pain Maldigestion Weight loss Glucose intolerance Older age	Alcohol / Smoking Hypertriglyceridemia Other metabolic / drugs AP / RAP Obstruction benign anatomic change Tumor	CT scan EUS (+/- FNA)	High amylase/lipase High triglycerides High IgG4 High glucose Low vitamins (ADK B12) Tumor markers	
b	Family history Early age of onset CF organ involvement Syndromic features	Genetic Testing (Genetic counseling: risk-based) Other toxic / metabolic risks	sMRCP	Sweat Chloride Exocrine function test	
c	IBD or evidence of IgG4 disease Clinical response to Rx? Pain management with antioxidants Improved digestion with PERT Steroid trial for AIP Type 2	Known causes ruled out / unlikely Expand differential diagnosis Initiate low-risk therapy (lifestyle, antioxidants) Consider referral		Histology	

Genetic Testing

- Obtain in patients with clinical evidence of a pancreatitis-associated disorder or CP of unclear etiology, especially in patients <35
- Goal: to assist in decision making and to prevent the development of irreversible CP. May affect treatment strategies (such as CFTR-related disorders)
- Can prevent exhaustive, invasive testing
- Can inform decisions on more radical therapy such as total pancreatectomy
- *At minimum check:* ***PRSS1, SPINK1, CFTR, and CTRC***; more extended panels available

Management

- EtOH and tobacco cessation
- Use caution in interventional procedures if active EtOH use, unless urgent/emergent
- Surgical intervention over endoscopic therapy in patients with obstructive CP for pain relief if 1st line endoscopic approaches for drainage are unsuccessful
- Consider celiac plexus block for pain
- Consider antioxidant therapy for pain
- Do not use pancreatic enzyme supplementation for pain
- Opiates may be considered in patients in whom other therapeutic options have failed
- Surgical referral for refractory pain