ACG International Webinar Series:
Diagnosis and Management of Chronic Pancreatitis

Hosted by the Italian Society of Gastroenterology (SIGE)

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Special Guest: Luca Frulloni, MD, PhD
Full Professor of Gastroenterology
Head of Gastroenterological Unit, Department of Medicine, Institute of Pancreas
University of Verona
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Participating in the Webinar

All attendees will be muted and will remain in Listen Only Mode.

Type your questions here so that the moderator can see them. Not all questions will be answered but we will get to as many as possible.
Diagnosis and Management of Chronic Pancreatitis

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Objectives

1. Designing Clinical Guidelines
2. Diagnosis
3. Etiology and Natural History
4. Management of Pain
5. Management of EPI
Case Presentation

Chief Complaint: Chronic abdominal pain

History of Present Illness:
- 42 year old male
- Insidious onset of pain for several years
- Epigastric with radiation to the back
- 20-30 ounces of alcohol daily
- Unremarkable lab testing
- Normal fecal elastase
- CFTR ΔF508 heterozygote

Case Presentation

Serology: Normal amylase, lipase, TTG, IgG4, CA 19-9
Case Presentation

4 EUS Morphologic Criteria
- Hyperechoic duct wall (body)
- Hyperechoic foci (head, body, tail)
- Hyperechoic strands (head, body, tail)
- Lobularity in body and tail

How does one interpret these results?
Does he have chronic pancreatitis?
How should be treated?
Designing Clinical Guidelines

1. Designing Clinical Guidelines

2. Diagnosis

3. Etiology and Natural History

4. Management of Pain

5. Management of EPI
Designing Clinical Guidelines

**Literature Search** – major databases from 1946-present

**Best evidence** – i.e. RCTs, systematic review and meta-analysis

**PICO questions for answerable questions**
- Population/Problem
- Intervention
- Comparison
- Outcome

### Table 1. PICO questions that served as the basis for recommendations and key concepts

<table>
<thead>
<tr>
<th>Diagnosis</th>
<th>PICO Questions</th>
</tr>
</thead>
<tbody>
<tr>
<td>Question: Should cross-sectional imaging (CT or MRI) or ERCP be used to diagnose CP in patients suspected of having CP?</td>
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**American College of Gastroenterology**
Designing Clinical Guidelines

Once you have designed the PICO questions...

- Evaluate the literature to answer your questions

- If you have enough evidence to answer the questions, start the GRADE evaluation process

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A few reminders about guidelines...

- They are limited by the amount of clinical trial evidence available

- There are multiple types of guidelines – beware of those that do not follow the GRADE system (i.e. beware of expert opinion)

- Not all important clinical questions can be answered – or even addressed – if using evidence-based guidelines
Designing Clinical Guidelines

Two Types of Statements

1. Recommendations
   - Evidence
   - Grade System

2. Key Concepts
   - Not amenable to Grade
   - Often expert opinion

Objectives

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Diagnosis

Recommendation Statements

1. We recommend computed tomography (CT) or MRI for the first-line diagnosis of CP. Either test should be the first choice for the diagnosis of CP. Endoscopic ultrasonography (EUS), because of its invasiveness and lack of specificity, should be used only if the diagnosis is in question after cross-sectional imaging is performed (strong recommendation, low quality of evidence).

EUS Diagnosis: The Perfect Storm

- No gold standard
- Highly sensitive test
- Confusing nomenclature
- Wide interobserver variation
- Lack of specificity
- Increasing availability
- Heavy reliance on expert opinion
Diagnosis

Recommendation Statements

2. We suggest performing secretin-enhanced magnetic resonance cholangiopancreatography (s-MRCP) when the diagnosis of CP following cross-sectional imaging or EUS is not confirmed and the clinical suspicion remains high (conditional recommendation, low quality of evidence).

3. We suggest histological examination as the gold standard to diagnose CP in high-risk patients when the clinical and functional evidence of CP is strong, but imaging modalities are inconclusive (conditional recommendation, very low quality of evidence).

**Diagnosis**

**Key Concepts**

1. Pancreatic function testing is an important means of diagnosing EPI; however, its role in establishing the diagnosis of CP is complementary.

![Diagram showing the diagnostic algorithm for chronic pancreatitis.](image)
Objectives

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Etiology and Natural History

Recommendation Statements

4. We recommend genetic testing in patients with clinical evidence of a pancreatitis-associated disorder or possible CP in which the etiology is unclear, especially in younger patients (strong recommendation, low quality of evidence).

Table 7. Summary of genetic polymorphisms implicated in CP (112, 113)

<table>
<thead>
<tr>
<th>Polymorphic gene</th>
<th>Inheritance pattern</th>
<th>Molecular functional consequence</th>
<th>Clinical manifestations</th>
</tr>
</thead>
<tbody>
<tr>
<td>ARH (arachidonic acid receptor)</td>
<td>Autosomal dominant</td>
<td>Associated with severe pancreatitis</td>
<td></td>
</tr>
<tr>
<td>PRKCI (protein kinase C)</td>
<td>Autosomal dominant</td>
<td>Associated with severe pancreatitis</td>
<td></td>
</tr>
<tr>
<td>CYP2C19 (cytochrome P450)</td>
<td>Autosomal dominant</td>
<td>Associated with severe pancreatitis</td>
<td></td>
</tr>
<tr>
<td>TTR (transferrin receptor)</td>
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**Etiology and Natural History**

**Recommendation Statements**

5. We recommend alcohol cessation in patients with CP (strong recommendation, very low quality of evidence).

6. We recommend smoking cessation in patients with CP (strong recommendation, very low quality of evidence).

**Key Concepts**

2. In patients with clinical features of CP, a comprehensive review of all risk factors should be performed. This provides information on the underlying mechanisms, identifies both fixed and modifiable risk factors, identifies potential targets for therapies, and provides clinically relevant prognostic information.

3. Identification of the disorders(s) underlying pancreatic inflammation is important in predicting progression to CP.

4. The development of DM in CP is most likely related to duration of disease, although other etiologic factors such as body mass index and smoking status may incur an increased risk.

5. There is a lack of evidence to suggest that performing screening examinations on patients with CP to detect pancreatic malignancy is beneficial.
Objectives

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Management of Pain

Recommendation Statements

7. We recommend surgical intervention over endoscopic therapy in patients with obstructive CP for the long-term relief of pain if first-line endoscopic approaches to pancreatic drainage have been exhausted or unsuccessful (strong recommendation, moderate quality of evidence).
Management of Pain

Recommendation Statements

8. We suggest considering the use of antioxidant therapy for CP with pain, although the benefit of pain reduction is likely limited (conditional recommendation, moderate quality of evidence).

9. We do not suggest the use of pancreatic enzyme supplements to improve pain in CP (conditional recommendation, low quality of evidence).
10. We suggest considering celiac plexus block for treatment of pain in CP (conditional recommendation, very low quality of evidence).

Management of Pain

Key Concepts

6. Performing elective interventional procedures on patients who are actively using alcohol should be considered cautiously. Patients requiring urgent or emergent procedures for complications of CP should be considered separately.

7. Opiates may be considered to treat painful CP only in patients in whom all other reasonable therapeutic options have been exhausted.

8. TPIAT should be reserved for highly selected patients with refractory chronic pain in which all other symptom control measures have failed.
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Management of EPI

Recommendation Statements

11. We suggest PERT in patients with CP and EPI to improve the complications of malnutrition (conditional recommendation, low level of evidence).
Management of EPI

Key Concepts

10. Patients with CP should have periodic evaluation for malnutrition, including tests for osteoporosis and fat-soluble vitamin deficiency.

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Future Areas of Investigation

Investigate the Mechanistic Definition of CP...

Definition worldwide (15,16). The Mechanistic Definition affirms the characteristics of end-stage disease as pancreatic atrophy, fibrosis, pain syndromes, duct distortion and strictures, calcifications, pancreatic exocrine dysfunction, pancreatic endocrine dysfunction, and dysplasia, but also addresses the disease mechanism as 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. The definition is linked to a progressive model to...

Future Areas of Investigation

Further comparative effectiveness treatment trials...

Endoscopic versus Surgical Drainage of the Pancreatic Duct in Chronic Pancreatitis

- Endoscopic approach
- Surgical approach
- Comparative effectiveness
- Outcome measures
- Cost analysis
- Long-term follow-up
Future Areas of Investigation

A reckoning of how these patients are demonized, mistreated, and cared for by our profession...

Thank You

“Man cannot discover new oceans unless he has the courage to lose sight of the shore”

- Andre Gide
1947 Nobel prize for literature