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Triggers and Treatment of Acute Pancreatitis

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University of Florida
Disclosures

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Disclosures

Rick Davis, PA-C
No financial relationships to disclose.
Acute Pancreatitis: Inflammatory Disorder of the Pancreas

- Acute pancreatitis
- Acute relapsing pancreatitis
- Acute on chronic pancreatitis
- Among most common GI disorders to cause hospitalization
- Global incidence of 34/100,000 person-years
Acute Pancreatitis: Etiologies

- Gallstone
- EtOH
- Trauma (e.g., ERCP, surgical resection, biopsy)
- Malignant/pre-malignant lesions
- Metabolic (hypertriglyceridemia; hypercalcemia)
Acute Pancreatitis: Etiologies (Cont’d)

- Genetic: PRSS1, SPINK1, CFTR
- Medications: e.g., mesalamine, azathioprine, losartan
- Infections: viral, bacterial, parasitic
- Idiopathic
Acute Pancreatitis: Pathophysiology

- Pathologic elevation of Ca++ concentration in acinar cells
- Mediates pro-cell death, pro-inflammatory pathways
- Activates NFkB and mitochondrial dysfunction
- Ductal obstruction with gallstones or ERCP can cause increased Ca++ entry to cells via plasma membrane receptors activated by pressure

Acute Pancreatitis: Pathophysiology Ca++ Mediated Mitochondrial Dysfunction and Cell Death
Immune Response to Acinar Cell Injury and Necrosis in Acute Pancreatitis

Acute Pancreatitis: Clinical Presentation

Acute onset of epigastric abdominal pain
  – Sharp with radiation to back and sudden onset frequently with biliary cause
  – Indolent, aching pain frequently with EtOH, metabolic

Nausea +/- vomiting

Anorexia
Acute Pancreatitis: Diagnostic Criteria
Revised Atlanta Classification (2012)

• Two of three of following:
  • Pancreatic enzymes, amylase/lipase > 3x ULN
  • Typical abdominal pain of acute pancreatitis
  • Findings of acute pancreatitis on cross-sectional imaging
Revised Acute Pancreatitis: Types
Atlanta Classification

- Interstitial edematous pancreatitis
  - Diffuse or localized enlargement of pancreas
  - Homogenous enhancement of parenchyma
  - Peripancreatic fluid collections
    - < 4 wks: Adjacent to pancreas (APFC)
    - > 4 wks: Pseudocyst

A 63-Year-Old Man With Acute Interstitial Oedematous Pancreatitis
Revised Acute Pancreatitis: Types
Atlanta Classification

• Necrotizing pancreatitis:
  – Necrosis of parenchyma +/- peripancreatic tissue
  – Variable contrast enhancement first few days
  – Non-enhancing areas > 1 wk considered necrosis

• Collections:
  – < 4 wk: Acute Necrotizing Collection (ANC)
    • Pancreatic/peripancreatic tissues; heterogenous non-liquid density, locations
  – > 4 wk: Walled Off Necrosis (WON)
    • Mature, encapsulated, well-defined wall, heterogenous liquid/non-liquid

(A–C) Three Different Patients With Walled-Off Necrosis (WON) After an Acute Attack of Necrotising Pancreatitis
Acute Pancreatitis: Grades of Severity
Revised Atlanta Criteria

• Mild:
  – No organ failure
  – No local or systemic complications

• Moderately Severe:
  – Organ failure, resolves < 48h
  – Local or systemic complications, no persistent organ failure

• Severe:
  – Persistent organ failure (> 48h); single or mult-organ failure
Acute Pancreatitis: Prediction of Severity

- SIRS: Systemic Inflammatory Response Syndrome
- BISAP: Bedside Index for Severity in Acute Pancreatitis
- APACHE II: Acute Physiology and Chronic Health Evaluation (ICU patients, not specific to acute pancreatitis)
- Ranson criteria (48h after admission)
Systemic Inflammatory Response Syndrome (SIRS) is the occurrence of at least two of the following criteria: fever $>38.0^\circ C$ or hypothermia $<36.0^\circ C$, tachycardia $>90$ beats/minute, tachypnea $>20$ breaths/minute, leucocytosis $>12\times10^9/l$ or leucopenia $<4\times10^9/l$.
### Table 2. Comparison of APACHE II, BISAP, and Ranson Scores Based on the Revised Atlanta Classification Definitions of Severity

<table>
<thead>
<tr>
<th>Variables</th>
<th>APACHE II</th>
<th>BISAP (2008, Gut)</th>
<th>Ranson</th>
</tr>
</thead>
<tbody>
<tr>
<td>Admission:</td>
<td>Age &gt; 55 y</td>
<td>Age &gt; 55 y</td>
<td>Age &gt; 55 y</td>
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<tr>
<td></td>
<td>WBC count &gt; 16,000/μL</td>
<td>Lactate dehydrogenase &gt; 350 IU/L</td>
<td>AST &gt; 250 IU/</td>
</tr>
<tr>
<td></td>
<td>Glucose &gt; 260 mg/dl</td>
<td>Within 48 h:</td>
<td>Fluid loss &gt; 6 L</td>
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<tr>
<td></td>
<td>Fall in hematocrit &gt; 10%</td>
<td>Increase in BUN &gt; 5 mg/dl</td>
<td>Base deficit &gt; 4 mEq/L</td>
</tr>
<tr>
<td></td>
<td>Calcium &lt; 8 mg/dl</td>
<td>Pao2 &lt; 60 mm Hg</td>
<td>Fluid loss &gt; 6 L</td>
</tr>
<tr>
<td></td>
<td>Pao2 &lt; 60 mm Hg</td>
<td>Hospital acuity</td>
<td>Base deficit &gt; 4 mEq/L</td>
</tr>
<tr>
<td></td>
<td>Acute kidney failure</td>
<td>Hospital acuity</td>
<td>Base deficit &gt; 4 mEq/L</td>
</tr>
<tr>
<td></td>
<td>Hemotocrit</td>
<td>Hospital acuity</td>
<td>Base deficit &gt; 4 mEq/L</td>
</tr>
<tr>
<td></td>
<td>WBC count</td>
<td>Hospital acuity</td>
<td>Base deficit &gt; 4 mEq/L</td>
</tr>
<tr>
<td></td>
<td>Glasgow Coma Scale</td>
<td>Hospital acuity</td>
<td>Base deficit &gt; 4 mEq/L</td>
</tr>
<tr>
<td></td>
<td>Fio2</td>
<td>Hospital acuity</td>
<td>Base deficit &gt; 4 mEq/L</td>
</tr>
<tr>
<td>Original purpose</td>
<td>Severity of disease and mortality in ICU patients</td>
<td>Prediction of mortality in AP</td>
<td>Prediction of mortality in AP</td>
</tr>
<tr>
<td>Prediction of severity, AUC (SE)22</td>
<td>Score ≥ 3</td>
<td>Score ≥ 3</td>
<td>Score ≥ 3</td>
</tr>
<tr>
<td>• Sensitivity (95% CI)</td>
<td>0.83 (0.77-0.88)</td>
<td>0.51 (0.43-0.60)</td>
<td>0.66 (0.59-0.72)</td>
</tr>
<tr>
<td>• Specificity (95% CI)</td>
<td>0.59 (0.56-0.63)</td>
<td>0.91 (0.89-0.92)</td>
<td>0.76 (0.76-0.81)</td>
</tr>
<tr>
<td>Prediction of mortality, AUC (SE)22</td>
<td>Score ≥ 3</td>
<td>Score ≥ 3</td>
<td>Score ≥ 3</td>
</tr>
<tr>
<td>• Sensitivity (95% CI)</td>
<td>0.83 (0.16)</td>
<td>0.87 (0.03)</td>
<td>0.92 (0.05)</td>
</tr>
<tr>
<td>• Specificity (95% CI)</td>
<td>0.93 (0.77-1.00)</td>
<td>0.68 (0.63-0.73)</td>
<td>0.93 (0.78-0.99)</td>
</tr>
<tr>
<td>Advantages</td>
<td>Can be calculated within 24 h</td>
<td>5 Variables</td>
<td>Comprehensive</td>
</tr>
<tr>
<td></td>
<td>• 5 Variables</td>
<td>• Easy to calculate (1 point per variable)</td>
<td>• Specific to AP</td>
</tr>
<tr>
<td></td>
<td>• Can be calculated within 24 h</td>
<td>• Can be calculated within 24 h</td>
<td>• Specific to AP</td>
</tr>
<tr>
<td>Limitations</td>
<td>• Designed for patients admitted to ICUs</td>
<td>• Lower sensitivity and specificity compared to APACHE II</td>
<td>• At least 48 h to calculate score</td>
</tr>
<tr>
<td></td>
<td>• Large set of mandatory variables</td>
<td>• Not specific to AP</td>
<td>• All data points not collected routinely in non-ICU patients</td>
</tr>
</tbody>
</table>

Abbreviations: AP, acute pancreatitis; APACHE II, Acute Physiology and Chronic Health Evaluation II; AST, aspartate aminotransferase; AUC, area under curve; BISAP, Bedside Index of Severe Acute Pancreatitis; BUN, blood urea nitrogen; Fio2, fraction of inspired oxygen; ICU, intensive care unit; Pao2, partial pressure of arterial oxygen; SIRS, systemic inflammatory response syndrome; WBC, white blood cell. Comparison of APACHE II, BISAP, and Ranson Scores Based on the Revised Atlanta Classification Definitions of Severity. Date of download: 7/29/2021. Copyright 2021 American Medical Association. All Rights Reserved. JAMA. 2021;325(4):382-390. doi:10.1001/jama.2020.20317.
Acute Pancreatitis: BISAP Bedside Index for Severity in Acute Pancreatitis Score

- BUN > 25 mg/dl
- Impaired mental status
- > 2 SIRS criteria
- Age > 60
- Pleural effusion present
- Score >/= 3 increased risk of severe pancreatitis; specific to acute pancreatitis [sens 0.51; spec 0.91]
Acute Pancreatitis: BISAP Score

- Developed in 2008
- Specific for acute pancreatitis
- Score $\geq 3$ associated with developing organ failure and pancreatic necrosis
- Lowest score with $< 1\%$ mortality
- Highest score with $> 20\%$ mortality
Time Course and Management of Acute Pancreatitis


Figure Legend:
Timeline, Manifestations, and Management of Acute Pancreatitis. SIRS indicates systemic inflammatory response syndrome.
A Review

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Acute Pancreatitis: Management

• Fluid resuscitation to restore tissue perfusion
  – Recent data suggesting Lactated Ringers solution superior to NS, [weak/moderate evidence]
  – Monitor VS, measure urine output, BUN, Hct

• Nutritional support
  – Enteral nutrition as soon as tolerated with low fat oral diet [AGA recs within 24h] if severe, n-g or n-j tube feeds
  – Prevent bacterial translocation, infection
### Table 3. Comparison of Guidelines for Fluid Resuscitation, Nutrition, and Timing of Cholecystectomy

<table>
<thead>
<tr>
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</thead>
<tbody>
<tr>
<td>Rate and/or targets of intravenous fluid resuscitation</td>
<td>Moderate-quality evidence Goal-directed intravenous fluid therapy with 5-10 ml/kg/h</td>
<td>Very low quality of evidence Goal-directed therapy for fluid management No recommendation on rate, volume, or duration</td>
<td>Moderate-quality evidence Bolus and maintenance fluid resuscitation with titration according to interval assessment of vital signs, urine output, BUN, and hematocrit during the first 48 h No recommendation on rate or volume</td>
<td>Quality of evidence: B&lt;sup&gt;a&lt;/sup&gt; ≥3 ml/kg/h, should be initiated unless prohibitive comorbidities exist (e.g., heart or kidney failure) Trend BUN, hematocrit, creatinine every 6-12 h for the first 24-48 h</td>
</tr>
<tr>
<td>Type of fluid for initial resuscitation</td>
<td>Moderate quality of evidence Lactated Ringer solution</td>
<td>Low quality of evidence No recommendation</td>
<td>Moderate-quality evidence Lactated Ringer solution unless contraindicated</td>
<td>Quality of evidence: B&lt;sup&gt;a&lt;/sup&gt;</td>
</tr>
<tr>
<td>Timing of enteral nutrition</td>
<td>Moderate quality of evidence In mild AP, oral feedings can be restarted once abdominal pain is decreasing and inflammatory markers are improving Moderate-quality evidence Early nutrition within 24 h</td>
<td>Moderate quality of evidence High-quality evidence Within 48-72 h unless it is not tolerated or is contraindicated (ie, bowel obstruction or paralytic ileus)</td>
<td>Quality of evidence: B&lt;sup&gt;a&lt;/sup&gt; In mild AP, oral feedings should be started within 24 h of symptom control</td>
<td></td>
</tr>
<tr>
<td>Route of nasoenteral nutrition (nasogastric vs nasojejunal)</td>
<td>High-quality evidence Nasogastric or nasojejunal</td>
<td>Low-quality evidence Nasogastric or nasojejunal for predicted severe or necrotizing AP</td>
<td>Nasogastric or nasojejunal&lt;sup&gt;a&lt;/sup&gt;</td>
<td>Quality of evidence: B&lt;sup&gt;a&lt;/sup&gt; Nasojejunal nutrition for severe AP if oral nutrition not tolerated within 3-5 d</td>
</tr>
<tr>
<td>Type of nutrition</td>
<td>Moderate-quality evidence Elemental or polymeric enteral nutrition formulations</td>
<td>No recommendation</td>
<td>High-quality evidence Low-fat solid diet</td>
<td>No recommendation</td>
</tr>
<tr>
<td>Timing of cholecystectomy for biliary AP</td>
<td>Low-quality evidence Initial admission for mild AP Low-quality evidence Cholecystectomy in biliary AP complicated by collections should be deferred until collections resolve or if they persist beyond 6 weeks</td>
<td>Moderate-quality evidence Initial admission</td>
<td>High-quality evidence Surgery consultation to consider cholecystectomy prior to discharge Moderate-quality evidence Cholecystectomy in biliary AP complicated by necrosis or collections should be deferred until inflammation subsides or collections resolve/stabilize</td>
<td>Quality of evidence: B&lt;sup&gt;a&lt;/sup&gt; Within 2 wk for mild AP</td>
</tr>
</tbody>
</table>

Abbreviations: ACG, American College of Gastroenterology; AGA, American Gastroenterological Association; AP, acute pancreatitis; APA, American Pancreatic Association; BUN, blood urea nitrogen; IAP, International Association of Pancreatology.

<sup>a</sup> Limited or conflicting evidence from single randomized trial or nonrandomized studies; <sup>b</sup> Quality of evidence for recommendation not provided.


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Acute Pancreatitis: Endoscopic Interventions

- ERCP: Sphincterotomy, stent placement for obstructive cholangitis, choledocholithiasis
- EUS-guided trans-gastric drainage of pseudocyst
- EUS-guided trans-gastric necrosectomy of Walled Off Necrosis (WON)
Endoscopic Management of Walled-Off Pancreatic Necrosis

Acute Pancreatitis: Clinical Pearls

- Confirm diagnosis at consultation of acute pancreatitis correctly
- Predict severity of disease
- Necrotizing pancreatitis can be a late complication
- Do initiate fluid resuscitation but monitor for fluid overload, I/Os
- Consider Lactated Ringers > NS if not contraindicated
- Don’t give empiric antibiotics, only if signs of infected necrosis
- Initiate low fat enteral feeding early as tolerated
Acute Pancreatitis: Clinical Pearls

- Treat underlying etiology early
- Repeat cross sectional imaging if clinical worsening
- Involve supervising gastroenterologist early especially if predictive scores or signs of severe disease and need for critical care
- Consult surgery for biliary etiology
- ERCP only if cholangitis/choledocholithiasis while hospitalized
Acute Pancreatitis: Sequelae

• Risk factors for recurrent pancreatitis:
  – EtOH acute pancreatitis
  – Biliary pancreatitis w/o cholecystectomy
  – Tobacco smoking

• Risk factors for progression to chronic pancreatitis:
  – Recurrent acute pancreatitis
  – Pancreatic necrosis
  – Tobacco smoking
  – EtOH acute pancreatitis


