Peri-pancreatic collections:
Update on disease classification and endoscopic therapy

Neil Gupta MD, MPH
Assistant Professor of Medicine
Division of Gastroenterology
Disclosures

• I have no disclosures.
Objectives

• Revised 2012 Atlanta Classification system

• Medical decision making concepts with regards to treatment

• Endoscopic therapies
Acute Pancreatitis

• Abdominal pain consistent with acute pancreatitis
  – Acute, severe, persistent epigastric pain
  – Often radiating to the back

• Lipase/amylase activity at least 3x upper limit of normal

• Radiologic findings of acute pancreatitis
Disease Onset

• Time of onset of abdominal pain

• Not time of hospital admission

• Documentation of time admission and time of transfer (outcomes monitoring)
Disease Sub-types

Interstitial edematous pancreatitis
• 90-95% of cases

Necrotizing pancreatitis
• 5-10% of cases
Interstitial Edematous Pancreatitis

• Diffuse (occ localized) pancreatic enlargement

• Homogenous enhancement on CECT

• Peri-pancreatic fat stranding

• Peri-pancreatic fluid can be present

• Clinical symptom resolution within 1 week
Interstitial Edematous Pancreatitis
Necrotizing Pancreatitis

- Pancreatic parenchyma and/or peri-pancreatic tissue
- Evolution over several days (disease under-staging)
- Variable natural history
- Higher intervention rates and increased morbidity and mortality
Atlanta Classification

• Originally in 1992
• Fluid collection descriptions were confusing and not universal

• Improvement in diagnostic imaging
• Better understanding of pathophysiology and disease outcomes

• Consistent, worldwide classification
Local Complications

• Acute peri-pancreatic fluid collection
• Pancreatic pseudocyst
• Acute necrotic collection
• Walled-off necrosis
Acute Peri-pancreatic Fluid Collection

- Peri-pancreatic fluid associated with interstitial edematous pancreatitis
- Within first 4 weeks of disease onset
- No peri-pancreatic necrosis
- No features of pseudocyst (encapsulation)
- No intra-pancreatic extension
Acute Peri-pancreatic Fluid Collection
Acute Peri-pancreatic Fluid Collection

Retrospective: 73 patients with APFC
- Rapid resolution: 68.6%
- Persistence but asymptomatic at 2 weeks: 13.7%
- Abdominal complication: 17.6%
  - Pseudocyst formation: 6.8%
  - Major complications: 6.8%

Acute Peri-pancreatic Fluid Collection

- Remain sterile
- Resolve spontaneously without intervention
- Persistent APFC can develop into pseudocysts
- Do not constitute severe pancreatitis
Acute Peri-pancreatic Fluid Collection
Pancreatic Pseudocyst

• Completely encapsulated collection of fluid
  – Well defined wall

• Minimal or no necrosis
  – Homogenous fluid density

• Can be partly or wholly intra-pancreatic

• Usually > 4 weeks since onset
  – Can occur within 1 week
Pancreatic Pseudocyst
Acute Necrotic Collection

• Variable amounts of fluid and necrosis
  – Heterogeneous and non-liquid densities

• Associated with necrotizing pancreatitis

• No definable encapsulating wall

• Intra or extra pancreatic
Acute Necrotic Collection
Acute Necrotic Collection
Acute Necrotic Collection
Walled-off Necrosis

• Pancreatic and/or peri-pancreatic necrosis and fluid
  – Heterogeneous with liquid and non-liquid densities

• Complete encapsulation

• Intra and/or extra pancreatic

• Usually > 4 weeks after onset
Walled-off Necrosis
Infected Necrosis

- Rare during the first week of disease
- No correlation with extent of necrosis
- Increased morbidity and mortality
- Extra-luminal gas
- Positive FNA
- “pancreatic abscess” no longer used
Infected Necrosis
Local Complications

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- Pancreatic pseudocyst
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Local Complications

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Local Complications

• Acute peri-pancreatic fluid collection
• Pancreatic pseudocyst
• Acute necrotic collection
• Walled-off necrosis

• Less spontaneous resolution
• Symptomatic
• Infection
• Main pancreatic duct disruption
Controversies

- Considerable overlap – IOA not determined
- Encapsulation can occur < 4 weeks
- Limitations in detecting solid debris
- How much solid debris to be called WON
- Still no breakthroughs in detecting infected necrosis
Local Complications

- Acute peri-pancreatic fluid collection
- Pancreatic pseudocyst
- Acute necrotic collection
- Walled-off necrosis
Indication for Intervention

- Infection – infected necrosis
- Luminal obstruction
- Biliary obstruction
- Recurrent acute pancreatitis
- Persistent pain
Timing of Intervention

• Sooner the intervention – poorer outcomes
  – Sicker patients (infected) require early intervention

• Poorly organized collections are more difficult to manage
  – Limits therapeutic options

• Wait until encapsulation if possible
Goals of Intervention

• Control source of infection
  – Provide flow

• Alleviate obstruction
  – May not need to remove all necrotic material immediately
Minimally Invasive Interventions

• Percutaneous drainage
• Trans-mural endoscopic drainage
• Laparoscopic drainage

• Retroperitoneal sinus tract endoscopy
  – Videoscope assisted retroperitoneal debridement
• Trans-mural endoscopic necrosectomy
• Laparoscopic necrosectomy
Percutaneous Approach

Advantages
• Least invasive for critically ill
• Drainage of infected fluid can aid healing

Disadvantages
• Multiple procedures with high morbidity
• Central necrosis cannot be curatively treated
• High risk for fistula formation
• High failure rate (up to 80%)
• Most need adjunct therapy
Endoscopic Approach

Advantages
• Low risk of fistula formation
• Less invasive and lower morbidity/mortality
• Can be done in poor surgical risk

Disadvantages
• Need encapsulation
• Local bleeding risk (up to 33%)
• Multiple procedures
Laparoscopic Approach

Advantages
• Completely treat disease
• Access to most areas commonly affected

Disadvantages
• More invasive compared to other approaches
• Safety of pneumoperitoneum in critically ill
• High risk of intraperitoneal infection transmission (up to 30%)
EUS guided trans-mural drainage

- EUS examination
EUS guided trans-mural drainage

- Needle aspiration
EUS guided trans-mural drainage

- Trans-gastric guidewire insertion
EUS guided trans-mural drainage

- Tract Dilation
EUS guided trans-mural drainage

• Trans-gastric stent placement
EUS guided trans-mural drainage

- Retrospective: 294 patients with pseudocyst or WON
- Treatment success at 8-12 weeks: 88%
- 4 (1.3%) perforations
- 7 (2.4%) bleeding
- 6 non-pancreatic related deaths

EUS guided trans-mural drainage

• RCT: EUS guided vs. surgical cyst-gastrostomy
• 36 patients randomized with PC > 6cm

• No difference in technical and treatment success
• No difference in complications

• Better QOL scores for EUS
• Shorter hospital LOS: 2 vs. 6 days
• Lower costs: $8195 vs. $22,475

Endoscopic Necrosectomy

- Retrospective: 104 patients with WON
- 5-34cm, 42% with suspected infection
- Complete resolution: 95/104 (91%)
- Average time to resolution: 4 months
- Median number of procedures: 3

Endoscopic Necrosectomy

- Retrospective: 104 patients with WON
- 5-34cm, 42% with suspected infection

- Complications 14%
  - 5 interval deaths (2 pancreatic related)
  - 2 non-resolving collections
  - 1 procedure bleeding requiring surgery
  - 1 procedure hypotension resulting in death

Endoscopic Necrosectomy

• Retrospective: 40 patients with WON
• Endoscopic vs. percutaneous first-line therapy

Endoscopic Necrosectomy

• Retrospective: 40 patients with WON
• Endoscopic vs. percutaneous first-line therapy
• Clinical success: 16/19 vs. 4/21, p<0.01

Endoscopic Necrosectomy


<table>
<thead>
<tr>
<th>Item</th>
<th>EN (n=19)</th>
<th>PCD (n=21)</th>
<th>p-value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Necrosectomy professional</td>
<td>2083 ± 294</td>
<td>1829 ± 186</td>
<td>0.46</td>
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<tr>
<td>Theatre, instruments, recovery</td>
<td>7916 ± 1050</td>
<td>7708 ± 1351</td>
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<td>Anesthesia</td>
<td>1502 ± 795</td>
<td>1134 ± 220</td>
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<td>ICU &amp; ventilation*</td>
<td>40</td>
<td>46,674 ± 21,331</td>
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<td>Floor &amp; nursing</td>
<td>12,469 ± 3145</td>
<td>23,352 ± 4926</td>
<td>0.077</td>
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<tr>
<td>Radiology*</td>
<td>2668 ± 859</td>
<td>15,809 ± 3111</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Labs, pathology*</td>
<td>3301 ± 731</td>
<td>23,755 ± 7612</td>
<td>0.015</td>
</tr>
<tr>
<td>Pharmacy*</td>
<td>1303 ± 431</td>
<td>11,972 ± 3312</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Blood bank*</td>
<td>181 ± 89</td>
<td>4591 ± 1343</td>
<td>&lt;0.01</td>
</tr>
<tr>
<td>Nutrition*</td>
<td>175 ± 123</td>
<td>2894 ± 974</td>
<td>&lt;0.01</td>
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<tr>
<td>Physical, speech therapy*</td>
<td>60 ± 33</td>
<td>746 ± 249</td>
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<td>Hemodialysis</td>
<td>0</td>
<td>734 ± 635</td>
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<tr>
<td>Cardiology</td>
<td>0</td>
<td>2515 ± 1986</td>
<td>0.24</td>
</tr>
<tr>
<td>Endoscopy</td>
<td>0</td>
<td>730 ± 477</td>
<td>0.15</td>
</tr>
<tr>
<td>Total*</td>
<td>39,325 ± 5816</td>
<td>144,357 ± 37,342</td>
<td>0.011</td>
</tr>
<tr>
<td>Charge until resolution</td>
<td>51,886 ± 5850</td>
<td>219,751 ± 42,149</td>
<td>&lt;0.01</td>
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<tr>
<td>Related admissions</td>
<td>48,623 ± 18,878</td>
<td>34,116 ± 28,096</td>
<td>0.68</td>
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</tbody>
</table>
**Endoscopic Necrosectomy**

- Retrospective: 50 patients with WON
- Endoscopic vs. surgical first-line therapy

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<tbody>
<tr>
<td>Gender</td>
<td>11M/8F</td>
<td>14M/5F</td>
<td>0.50</td>
</tr>
<tr>
<td>Age</td>
<td>54.4 ± 3.1</td>
<td>54.3 ± 2.8</td>
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<td>Charlson comorbidity</td>
<td>1.53 ± 0.5</td>
<td>1.11 ± 0.3</td>
<td>0.46</td>
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<tr>
<td>APACHE II</td>
<td>6.40 ± 1.0</td>
<td>7.31 ± 1.1</td>
<td>0.55</td>
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<tr>
<td>Preprocedure collection size (mL)</td>
<td>1999 ± 986</td>
<td>1314 ± 338</td>
<td>0.49</td>
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</tbody>
</table>

Endoscopic Necrosectomy

• Retrospective: 50 patients with WON
• Endoscopic vs. surgical first-line therapy

• No difference in clinical success
• No difference in treatment complications

## Endoscopic Necrosectomy

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<td>3171 ± 398</td>
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<td>40</td>
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<td>12,469 ± 3145</td>
<td>29,661 ± 5886</td>
<td>0.02</td>
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<td>Radiology</td>
<td>2668 ± 859</td>
<td>9107 ± 2074</td>
<td>&lt;0.01</td>
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<td>4820 ± 1427</td>
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<td>1592 ± 403</td>
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<td>0</td>
<td>200</td>
<td>-</td>
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<td>0</td>
<td>256</td>
<td>-</td>
</tr>
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<td>Endoscopy</td>
<td>0</td>
<td>264</td>
<td>-</td>
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<td><strong>Total</strong></td>
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<td><strong>Related admissions</strong></td>
<td><strong>48,623 ± 18,787</strong></td>
<td><strong>65,287 ± 26,167</strong></td>
<td><strong>0.62</strong></td>
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</table>

Step Up Therapy: PANTER

- RCT 88 patients with suspected or confirmed infected necrosis
- Step-up vs. primary open necrosectomy
- Percutaneous or endoscopic drainage
- Sinus tract endoscopy - VARD

Step Up Therapy: PANTER

Organ Failure
Pulmonary Failure
Pao$_2$ lower than 60 mm Hg despite fraction of inspired oxygen (FIO$_2$) of 30% or need for mechanical ventilation
Circulatory Failure
Circulatory systolic blood pressure below 90 mm Hg despite adequate fluid resuscitation or need for inotropic catecholamine support
Renal Failure
Creatinine level more than 2.0 mg/dL after rehydration or new need for hemofiltration or hemodialysis
Multiple Organ Failure
Failure of 2 or more organs at the same time

Major Complications
New-Onset Multiple Organ Failure
Multiple organ failure that had not been present in the 24 hours before randomization
Intra-abdominal Bleeding Requiring Intervention
Surgical, radiological, or endoscopic intervention
Enterocutaneous Fistula or Perforation of a Visceral Organ Requiring Intervention
Secretion of fecal material from a percutaneous drain or drainage canal after removal of drains or from a surgical wound; secretion comes from either the small or large bowel and is confirmed with imaging or during surgery and requires either surgical, radiological, or endoscopic intervention

Pancreatic Fistula
Output via a percutaneous or nasocystic drain or drainage canal after removal of percutaneous drains or from a surgical wound of any measurable volume of fluid with an amylase content greater than 3 times the serum amylase activity

Long-term Complications
New-Onset Diabetes
The need for insulin or oral antidiabetic drugs to treat diabetes—which was not present before pancreatitis—6 months after discharge
Use of Pancreatic Enzymes
The use of oral pancreatic enzyme supplementation to treat clinical symptoms of steatorrhea—which was not present before onset of pancreatitis—6 months after discharge
Persisting Fluid Collections
The presence of pancreatic or peripancreatic fluid collections on computed tomographic scan 6 months after discharge.

SI conversion factor: To convert creatinine from mg/dL to µmol/L, multiply by 88.4.

a Adapted from the 1992 Atlanta classification for acute pancreatitis. b Adapted from the International Study Group on Pancreatic Fistula Definition (ISGPF) criteria for postoperative pancreatic fistula.
Step Up Therapy: PANTER

• Primary end point: 40% vs. 69%, p<0.01
• New onset organ failure: 12% vs. 42%
• Incisional hernias: 7% vs. 24%
• New onset DM: 16% vs. 38%
• 35% required only percutaneous drainage

Step Up Therapy: PENGUIN

• RCT 22 patients with suspected or confirmed infected necrosis
• Endoscopic vs. VARD/laparoscopic

• Primary outcome: IL-6 levels
  – 2h, 5h, 24h, and 7 days

Step Up Therapy: PENGUIN

- RCT 22 patients with suspected or confirmed infected necrosis

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Pao₂ lower than 60 mm Hg despite fraction of inspired oxygen (FIO₂) of 30% or need for mechanical ventilation
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### Step Up Therapy: PENGUIN

<table>
<thead>
<tr>
<th></th>
<th>Surgical Necrosectomy (n = 10)</th>
<th>Endoscopic Transgastric Necrosectomy (n = 10)</th>
<th>Risk Difference (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Major complications or death, No. (%)&lt;sup&gt;a&lt;/sup&gt;</td>
<td>8 (80)</td>
<td>2 (20)</td>
<td>0.60 (0.16 to 0.80)</td>
<td>.03</td>
</tr>
<tr>
<td>Death, No. (%)</td>
<td>4 (40)</td>
<td>1 (10)</td>
<td>0.30 (−0.08 to 0.60)</td>
<td>.33</td>
</tr>
<tr>
<td>Major complications, No. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New-onset multiple organ failure&lt;sup&gt;c&lt;/sup&gt;</td>
<td>5 (50)</td>
<td>0 (0)</td>
<td>0.50 (0.12 to 0.76)</td>
<td>.03</td>
</tr>
<tr>
<td>Intra-abdominal bleeding requiring intervention</td>
<td>0 (0)</td>
<td>0 (0)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Enterocutaneous fistula or perforation of a visceral organ requiring intervention</td>
<td>2 (20)</td>
<td>0 (0)</td>
<td>0.20 (−0.11 to 0.51)</td>
<td>.47</td>
</tr>
<tr>
<td>Pancreatic fistula</td>
<td>7 (70)</td>
<td>1 (10)</td>
<td>0.60 (0.17 to 0.81)</td>
<td>.02</td>
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<tr>
<td>Long-term complications, No. (%)&lt;sup&gt;d&lt;/sup&gt;</td>
<td></td>
<td></td>
<td></td>
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</tr>
<tr>
<td>New-onset diabetes</td>
<td>3 (50)</td>
<td>2 (22)</td>
<td>0.28 (−0.17 to 0.63)</td>
<td>.33</td>
</tr>
<tr>
<td>Use of pancreatic enzymes</td>
<td>3 (50)</td>
<td>0 (0)</td>
<td>0.50 (0.07 to 0.81)</td>
<td>.04</td>
</tr>
<tr>
<td>Persisting fluid collections&lt;sup&gt;e&lt;/sup&gt;</td>
<td>3 (50)</td>
<td>2 (22)</td>
<td>0.28 (−0.17 to 0.63)</td>
<td>.33</td>
</tr>
</tbody>
</table>

Take Home

• Know and use the Atlanta Classification system

• Local complications of pancreatitis
  – Multi-disciplinary approach
  – Buy time if possible
  – Step up therapy is here and probably is going to stay