Severe Acute, Necrotizing Pancreatitis: Optimal Treatment

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Nothing to disclose
Objectives

• Review evidence-based guidelines and new studies in the treatment of necrotizing pancreatitis.
• Discuss percutaneous, endoscopic and surgical techniques use in the management of necrotizing pancreatitis.
• Review optimal algorithms for diagnosis and management of necrotizing pancreatitis.
IAP/APA evidence-based guidelines for the management of acute pancreatitis

Working Group IAP/APA Acute Pancreatitis Guidelines

International Association of Pancreatolog...
Severe Pancreatitis

- Severe pancreatitis can be accompanied by profound SIRS and MOF
- Identical to sepsis
- Approx 10% of cases results in pancreatic necrosis
Diagnosis?

- CT scan: contrast enhanced
  - Arterial phase
  - Venous phase
- MRI
  - Gadolinium
Indications for imaging?

1) Diagnostic uncertainty
2) Confirmation of severity
3) Failure to respond to conservative treatment

• Ideal timing: 72-96 hours after onset of symptoms

(LOE Grade 1C, strong agreement)
Necrosis is Bad


<table>
<thead>
<tr>
<th></th>
<th>Edematous Pancreatitis N=118</th>
<th>Necrotic Pancreatitis N = 86</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pts MOF</td>
<td>0</td>
<td>30 (35%)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Pulm insuff</td>
<td>4 (3%)</td>
<td>54 (63%)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>AKI</td>
<td>1 (1%)</td>
<td>11 (13%)</td>
<td>&lt; 0.0017</td>
</tr>
<tr>
<td>Pressors</td>
<td>3 (3%)</td>
<td>20 (26%)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Sepsis</td>
<td>0</td>
<td>9 (10%)</td>
<td>&lt; 0.006</td>
</tr>
</tbody>
</table>
Necrosis as a Predictor?

- Severe pancreatitis can be accompanied by profound SIRS and MOF
- Identical to sepsis
- While there is an association between necrosis and MOF, it is not causal and cannot be used to guide management alone

Reality

- Sterile necrosis can be managed non-operatively - well

<table>
<thead>
<tr>
<th>Table 4. CHARACTERISTICS OF PATIENTS WITH STERILE AND INFECTED NECROSIS</th>
</tr>
</thead>
<tbody>
<tr>
<td></td>
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<tr>
<td>------------------</td>
</tr>
<tr>
<td>Female</td>
</tr>
<tr>
<td>Male</td>
</tr>
<tr>
<td>Mean age (range)</td>
</tr>
<tr>
<td>Biliary cause</td>
</tr>
<tr>
<td>Alcohol</td>
</tr>
<tr>
<td>Other or undefined cause</td>
</tr>
<tr>
<td>Mean serum c-reactive protein in mg/L (range)*</td>
</tr>
<tr>
<td>Mean Ranson score (range)</td>
</tr>
<tr>
<td>Mean APACHE II score (range)*</td>
</tr>
<tr>
<td>Mean hospital stay in days (range)</td>
</tr>
<tr>
<td>Surgical treatment (%)</td>
</tr>
<tr>
<td>Hospital deaths</td>
</tr>
</tbody>
</table>

IPN, infected pancreatic necrosis; SPN, sterile pancreatic necrosis.
* Peak value in the first week of disease.

Truth: Infected Necrosis is Worse

- Infected necrosis carries a high morbidity

<table>
<thead>
<tr>
<th></th>
<th>Sterile Pancreatic Necrosis N=57</th>
<th>Infected Pancreatic Necrosis N = 86</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Pts MOF</td>
<td>10 (18%)</td>
<td>20 (69%)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Pulm insuff</td>
<td>27 (47%)</td>
<td>27 (93%)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>AKI</td>
<td>3 (5%)</td>
<td>8 (28%)</td>
<td>&lt; 0.01</td>
</tr>
<tr>
<td>Pressors</td>
<td>5 (9%)</td>
<td>15 (52%)</td>
<td>&lt; 0.0001</td>
</tr>
<tr>
<td>Sepsis</td>
<td>1 (2%)</td>
<td>8 (28%)</td>
<td>&lt; 0.01</td>
</tr>
</tbody>
</table>

Truth: Infected Necrosis is Worse

• Infected necrosis carries a high mortality
  – 80% of patients who died associated with infected necrosis

Factors associated with mortality:

<table>
<thead>
<tr>
<th>% necrosis</th>
<th>Mortality</th>
</tr>
</thead>
<tbody>
<tr>
<td>30%</td>
<td>&lt;10% mortality</td>
</tr>
<tr>
<td>50%</td>
<td>25% mortality</td>
</tr>
<tr>
<td>Near total</td>
<td>&gt;50%</td>
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</tbody>
</table>

Extrapancreatic necrosis: 34% (vs. 16%)
Pancreatic ascites: 37% (vs. 9%)
Bacteria infection: 32% (vs. 10%)

Thus: Aggressive Management?

• Intervention / necrosectomy for infected pancreatic necrosis in critically ill patients.
  – Aimed at source control
Indications for interventions


1) Clinical suspicion of or documented infection with clinical deterioration (preferably after several weeks).
2) In the absence of documented infection, ongoing organ failure several weeks after onset of symptoms.

(LOE Grade 1C, strong agreement)
To aspirate or not to aspirate, that is the question…. 

1) Infection can be confirmed by FNA; there is a risk of false negative.
2) Routine aspiration is not indicated (clinical and imaging signs are often enough).

(LOE Grade 1C, strong agreement)
Identification of Infected Necrosis

• Clinical signs
  – Persistent fever
  – Inflammatory markers

• Imaging signs
  – Gas in peri-pancreatic tissue
Is Culture Sampling Reliable?

- **Yes**
  - 27 of 28 patients correctly diagnosed with pre-op FNA sampling

<table>
<thead>
<tr>
<th>Number Aspirations</th>
<th>Sterile necrosis 15 patients</th>
<th>Infected necrosis 28 patients</th>
</tr>
</thead>
<tbody>
<tr>
<td>1</td>
<td>12</td>
<td>16</td>
</tr>
<tr>
<td>2</td>
<td>3</td>
<td>6</td>
</tr>
<tr>
<td>3</td>
<td>0</td>
<td>5</td>
</tr>
<tr>
<td>&gt; 3</td>
<td>0</td>
<td>1</td>
</tr>
</tbody>
</table>
In whom does culture not inform?

- Patients with necrosis and intraperitoneal air on CT → necrosectomy
  - Not amenable to percutaneous drainage

- Hemodynamically stable (afebrile, chronically unwell) patients with CT finding of necrosis → expectant management
What about sterile pancreatic necrosis? Aggressive Management?

- Invasive intervention for pancreatic necrosis in:
  - Critically ill patients?
    - Aimed at inflammation control
  - Chronically ill patients?
    - More anatomic considerations
1) Obstruction (gastric outlet, intestinal, biliary) due to mass effect.
2) Persistent symptoms (pain, “unwellness”).
3)Disconnected duct syndrome.

• For all recommended timing markedly later (>8 weeks).

(LOE Grade 2C, strong agreement)
Declining Morbidity and Mortality Rates in the Surgical Management of Pancreatic Necrosis

Thomas J. Howard · Jay B. Patel · Nicholas Zyromski · Kumar Sandrasegaran · Jian Yu · Atilla Nakeeb · Henry A. Pitt · Keith D. Lillemoe


<table>
<thead>
<tr>
<th></th>
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</thead>
<tbody>
<tr>
<td>Infected necrosis (%)</td>
<td>42 (76)</td>
<td>34 (72)</td>
<td>0.79</td>
</tr>
<tr>
<td>Symptomatic sterile necrosis (%)</td>
<td>11 (20)</td>
<td>12 (26)</td>
<td></td>
</tr>
<tr>
<td>Progressive organ failure (%)</td>
<td>2 (4)</td>
<td>1 (2)</td>
<td></td>
</tr>
<tr>
<td>Time to initial debridement (days±SD)</td>
<td>46±46</td>
<td>44±40</td>
<td>0.82</td>
</tr>
<tr>
<td>Reoperation rate (%)</td>
<td>37 (67)</td>
<td>32 (68)</td>
<td>0.93</td>
</tr>
<tr>
<td>Morbidity rate (%)</td>
<td>49 (89)</td>
<td>34 (72)</td>
<td>0.03</td>
</tr>
<tr>
<td>Pancreatic fistula rate (%)</td>
<td>27 (49)</td>
<td>28 (60)</td>
<td>0.29</td>
</tr>
<tr>
<td>Intensive care unit length of stay (days±SD)</td>
<td>13±25</td>
<td>9±13</td>
<td>0.33</td>
</tr>
<tr>
<td>Hospital length of stay (days±SD)</td>
<td>38±33</td>
<td>26±23</td>
<td>0.04</td>
</tr>
<tr>
<td>Mortality rate (%)</td>
<td>10 (18)</td>
<td>2 (4)</td>
<td></td>
</tr>
</tbody>
</table>
Improvement!

- Necrosectomy is best delayed until 4 weeks to allow delineation of and detachment of necrotic tissues
  
  Mortality 23% → 5%
  
  Mortality 75% → 45% → 8%
Timing of Intervention


1) Surgical necrosectomy (any method): after 4 weeks (if possible).

2) Endoscopic or radiologic intervention (any method): after 4 weeks (if possible).

- “Walled off”: euphemism for liquefied or actually debridable!

(LOE Grade 1C, strong agreement)
Typical presentation...

• 55 yo man presents to the ED with abdominal pain, nausea, weight loss
• Multiple recent hospitalizations at OSH over past 6 weeks for acute pancreatitis
• “No one wants to do anything!”
• PSHx: L Hip replacement, appy
• PMHx (chronic): HTN, IDDM, HLD, cholelithiasis
• PMHx (acute): DVT, recent AKI requiring short course of HD, ARDS with 3 day vent course
Open necrosectomy

- To OR
- Open debridement pancreatic bed, washout and wide drainage.
- Upper abdomen frozen (initial approach to lesser sac via the transverse mesocolon, then gastro-colic window)
- Gall bladder left in place (unapproachable)
- G-tube not possible (stomach would not come up)
- Closure over 4 large drains throughout retroperitoneum
Infected necrosis

- Fluid
  - HEAVY CITROBACTER YOUNGAE
  - HEAVY KLEBSIELLA PNEUMONIAE
  - HEAVY STAPHYLOCOCCUS SPECIES, COAGULASE NEGATIVE
  - HEAVY LACTOBACILLUS SPECIES

- Tissue
  - HEAVY KLEBSIELLA PNEUMONIAE
  - HEAVY ENTEROCOCCUS FAECALIS
  - HEAVY STAPHYLOCOCCUS LUGDUNENSIS
  - HEAVY PREVOTELLA SPECIES BETA LACTAMASE PRODUCING
  - HEAVY BACTEROIDES FRAGILIS GROUP BETA LACTAMASE PRODUCING
Post-op....

- Early ICU course: SIRS
- Weaned from vent by POD 4
- Early parenteral nutrition
- POD7: Biliary fluid in drains, Non-contrast CT shows no collections and excellent drainage
- POD10: Persistent low volume biliary drainage, PO contrast CT
Post-op....

- UGI confirm small leak from medial c-loop of duodenum
- Improving, moving bowels, low output from drains
- POD 34: hypotension, BRB from drains
- To SICU, stabilized, CT showed no blush
- Sentinel bleed: to angiography
- Severe irregularity of both GDA and splenic arteries
- Both embolized
Post-op....

- Persistent low volume bilious drainage
- PEG on POD 61
- Exchanged to PEG-J for feeding 13 days later
- Tolerating feeds no change in drainage
- POD 81: severe abdominal pain, WBC to the 40's, CT showing cecal pneumatosis
Post-op:

- To the OR emergently
- Upper abdomen still frozen
- No ischemia found
- Clearly septic
- Damage control, open abdomen, bowel edema from resuscitation
- ? Re-feeding cholecystitis, sepsis: Cholecystostomy
Post-op...

- Small bowel fistula (open abdomen complication)
- Several months: duodenal fistula closed, drains out, on TPN but taking PO
- Abdominal wound contraction
- 10/2012 ready for EC fistula takedown, abdominal wall reconstruction and CCY
Resolution...

- Returned to normal diet, activity
- Off TPN
- Significant DM
- Doing well
Complications…

- Mortality? NO
- Arterial pseudoaneurysm and bleed
- Enteric fistula
  - Duodenal (early)
  - Small bowel (late)
- Abdominal wall reconstruction
A Step-up Approach or Open Necrosectomy for Necrotizing Pancreatitis

<table>
<thead>
<tr>
<th>Outcome</th>
<th>Minimally Invasive Step-up Approach (N=43)</th>
<th>Primary Open Necrosectomy (N=45)</th>
<th>Risk Ratio (95% CI)</th>
<th>P Value</th>
</tr>
</thead>
<tbody>
<tr>
<td>Primary composite end point: major complications or death — no. (%)†</td>
<td>17 (40)</td>
<td>31 (69)</td>
<td>0.57 (0.38–0.87)</td>
<td>0.006</td>
</tr>
<tr>
<td>Secondary end points</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Major complication — no. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>New-onset multiple-organ failure or systemic complications‡</td>
<td>5 (12)</td>
<td>19 (42)</td>
<td>0.28 (0.11–0.67)</td>
<td>0.001</td>
</tr>
<tr>
<td>Multiple-organ failure</td>
<td>5 (12)</td>
<td>18 (40)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Multiple systemic complications</td>
<td>0</td>
<td>1 (2)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Intraabdominal bleeding requiring intervention</td>
<td>7 (16)</td>
<td>10 (22)</td>
<td>0.73 (0.31–1.75)</td>
<td>0.48</td>
</tr>
<tr>
<td>Enterocutaneous fistula or perforation of a visceral organ requiring intervention</td>
<td>6 (14)</td>
<td>10 (22)</td>
<td>0.63 (0.25–1.58)</td>
<td>0.32</td>
</tr>
<tr>
<td>Death — no. (%)</td>
<td>8 (19)</td>
<td>7 (16)</td>
<td>1.20 (0.48–3.01)</td>
<td>0.70</td>
</tr>
<tr>
<td>Other outcome — no. (%)</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Pancreatic fistula</td>
<td>12 (28)</td>
<td>17 (38)</td>
<td>0.74 (0.40–1.36)</td>
<td>0.33</td>
</tr>
<tr>
<td>Incisional hernia§</td>
<td>3 (7)</td>
<td>11 (24)</td>
<td>0.29 (0.09–0.95)</td>
<td>0.03</td>
</tr>
<tr>
<td>New-onset diabetes§</td>
<td>7 (16)</td>
<td>17 (38)</td>
<td>0.43 (0.20–0.94)</td>
<td>0.02</td>
</tr>
<tr>
<td>Use of pancreatic enzymes§</td>
<td>3 (7)</td>
<td>15 (33)</td>
<td>0.21 (0.07–0.67)</td>
<td>0.002</td>
</tr>
</tbody>
</table>
Current Best Practice for Intervention


1) Percutaneous or endoscopic drainage should be the first step.

2) This then is followed by step up to interventional necrosectomy if necessary (endoscopic or surgical).

(LOE Grade 1A, strong agreement)
Drain only

- 66 yo male vasculopath
- CAD, ESRD on peritoneal dialysis
- s/p EVAR
- Complicated by severe pancreatitis
- Early sepsis, MOF
Drain only
Drain only
Drain only

- Persistent moderate volume pancreatic rich fluid (200 cc/day) over approximately 8 weeks
- Converted to serous fluid
- Cavity self-sclerosed
- Drain ultimately removed
Endoscopic drainage

- 24 yo male with minimal history
- Presents with severe alcohol associated pancreatitis
- Chronically unwell
- Symptoms of poor gastric outlet
Endoscopic drainage
Endoscopic drainage
Endoscopic drainage
Video Assisted Retroperitoneal Debridement (VARDs)

- 61 yo male
- Hx of prior cholecystectomy
- s/p ERCP with perforation
- Further complicated by severe acute necrotizing pancreatitis.
Video Assisted Retroperitoneal Debridement (VARDs)
Video Assisted Retroperitoneal Debridement (VARDs)
Getting the Dead Out: Modern Treatment Strategies for Necrotizing Pancreatitis

Monica M. Dua · David J. Worhunsky · Sabina Amin · John D. Louie · Walter G. Park · George Triadafilopoulos · Brendan C. Visser

Fig. 6 Intraoperative pancreatic necrosectomy with a nephroscope aiming at creating adequate space within the necrotic cavity

Fig. 7 Intraoperative view of the necrotic cavity during MIRP debridement and lavage. After nephroscopic debridement, the nephrosopic sheaths are exchanged for laparoscopic ports to introduce working instruments for debridement under direct visual guidance

Dig Dis Sci 2014 Apr; [epub]
VARDs: Personal preferences

- Percutaneous drains placed
- Upsize to 20 french
- Cystoscopic set
- Urologic drapes, decubitus or semi-decubitus positions
- Ring clamps, Bowel clamp ("linen-shod"), Aortic cross-clamp (curved)
Video Assisted Retroperitoneal Debridement (VARDs)
Video Assisted Retroperitoneal Debridement (VARDs)

- Persistent pancreatic fistula
- Finally closed at 4 months
- Multiple bouts of sepsis
- Drain out, regular diet
Transluminal endoscopic step-up approach versus minimally invasive surgical step-up approach in patients with infected necrotising pancreatitis (TENSION trial): design and rationale of a randomised controlled multicenter trial [ISRCTN09186711]

Algorithm

- **Pancreatic necrosis on CT?**
  - Signs of infection? No
    - expectant management (with repeat imaging for evolution of clinical picture)
  - Signs of infection? Yes,
    - Is it <4 weeks? Yes
      - Consider course of abx
    - Is it <4 weeks? No
      - Endoscopic or perc drainage with abx
Algorithm

- **Pancreatic necrosis on CT?**
  - Signs of infection? No
    - expectant management (with repeat imaging for evolution of clinical picture)
  - Persistent unwellness, obstruction? Yes
  - Is it <8 weeks? Yes
    - Continue supportive care
  - Is it <8 weeks? No
    - Endoscopic or perc drainage with abx
Algorithm

- **Endoscopic or perc drainage**
  - Resolution of symptoms? Yes
    - Supportive care (i.e. drain / fistula management)
  - Resolution of symptoms? No
    - Consider further endoscopy / drainage or upsize
    - Consider necrosectomy (endo, VARDS, open)
Conclusion

• Principles for management of necrotizing pancreatitis are largely unchanged…
  – Supportive care
  – Sterile versus infected necrosis
  – Debridement and source control

• The approach continues to evolve…
  – Avoidance of massive insult
  – Source control with measured intervention