Diagnosis and therapy of acute pancreatitis

Marc G Besselink
HPB chirurg, AMC Amsterdam
m.g.besselink@amc.nl
Disclosure:

- No conflict of interest
Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus

Peter A Banks, Thomas L Bollen, Christos Dervenis, Hein G Gooszen, Colin D Johnson, Michael G Sarr, Gregory G Tsiotos, Santhi Swaroop Vege, Acute Pancreatitis Classification Working Group
IAP/APA Evidence-based Guidelines on the Management of Acute Pancreatitis
Original article

IAP/APA evidence-based guidelines for the management of acute pancreatitis

Working Group IAP/APA Acute Pancreatitis Guidelines

\(^{a,b,*,1}\)

\(^{a}\) International Association of Pancreatolgy, UNSW Clinical School Locked Bag 7103, Liverpool, BC NSW 1871, Australia

\(^{b}\) American Pancreatic Association, PO Box 14906, Minneapolis, MN 55414, USA

Search: IAP/APA

Search: pancreatitis
Diagnosis
Diagnosis acute pancreatitis

• Definition acute pancreatitis: 2 of these 3 criteria

1. clinical (upper abdominal pain)
2. laboratory (serum lipase / amylase >3x upper limit of normal)
3. and/or imaging (CT, MRI, ultrasonography) criteria.

Remarks:
• usually (>95%) imaging not required for diagnosis

(GRADE 1B, strong agreement)
Imaging in early phase?

- Indication for early ultrasonography:
  - Screening for biliary cause (gallstones, sludge)

- Indication for initial CT assessment:
  - Diagnostic uncertainty
  - Confirmation of severity
  - Failure to respond to conservative treatment

Optimal timing for initial CT assessment is at least 72-96 hrs after onset of symptoms

(GRADE 1C, strong agreement)
Diagnosis necr. pancreatitis

“Inflammation associated with pancreatic parenchymal necrosis and/or peripancreatic necrosis”

• CECT criteria:
  ▶ Lack of pancreatic parenchymal enhancement
  ▶ Presence of findings of peripancreatic necrosis

NB: pseudocyst acute pancreatitis <0.1%
Therapy
General, acute pancreatitis
General treatment

- Fluid
- Feeding
- ERCP / cholecystectomy
- Anti / pro-biotics
Fluid

- 5-10 ml/kg/h until goals have been reached
  - **Goals:** heart rate <120/min, MAP 65-85 mmHg, urine output >0.5-1 ml/kg/h.
  - Usually 2.5-4 L Ringer’s lactate will suffice in first 24hrs
  - High infusion with either 10-15 ml/kg/h or aiming at hematocrit <35% within 48hrs = **HIGHER MORTALITY**

Grade 2B, weak agreement
Feeding

- Mild pancreatitis: oral diet
- Predicted severe pancreatitis: oral diet, if no oral intake after 72-96 hrs, nasogastric or nasojejunal feeding tube

Grade 1B, strong agreement
No benefit of routine nasoenteral feeding <24hrs after diagnosis

Early versus On-Demand Nasoenteric Tube Feeding in Acute Pancreatitis


PYTHON trial
• Urgent ERCP is indicated in patients with biliary pancreatitis and cholangitis (GRADE 1B, strong agreement)

• ERCP is probably indicated in biliary pancreatitis with common bile duct obstruction (GRADE 1C, strong agreement)

• ERCP is not indicated in predicted mild biliary pancreatitis without cholangitis (GRADE 1A, strong agreement)

• ERCP is probably not indicated in predicted severe biliary pancreatitis without cholangitis (GRADE 1B, strong agreement)

Remark: currently no evidence regarding **timing** of ERCP in pts with predicted severe biliary pancreatitis without cholangitis
APEC trial

**Acute biliary Pancreatitis**: early ERC plus sphincterotomy versus Conservative treatment
APEC trial: PICO

- **Patients:** 232 patients with predicted severe biliary pancreatitis
- **Intervention:** ERC + sphincterotomy < 24 hrs
- **Comparison:** conservative treatment
- **Outcome:** major complications and death

Subgroup analysis for patients with/without cholestasis

29 Dutch hospitals 2013-2016

ISRCTN97372133
• Should the gallbladder be removed prior to discharge of a patient with mild biliary pancreatitis?

YES

NO
Timing of cholecystectomy following mild biliary pancreatitis
a randomized controlled multicenter trial

PONCHO trial
Patients: 266 patients with first episode mild biliary pancreatitis

Intervention: cholecystectomy <72 after randomization

Control: cholecystectomy 25-30dys after randomization

Outcome: re-admission for biliary complications or mortality

Randomization: when discharge was planned and expected <24-48hrs

23 Dutch hospitals 2010-2013
## PONCHO trial: results

<table>
<thead>
<tr>
<th></th>
<th>Same admission (N=128)</th>
<th>Interval (N=136)</th>
<th>Risk Ratio (95% CI)</th>
<th>P value</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Primary endpoint; No. (%)</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Acute readmission or mortality</td>
<td>6 (5)</td>
<td>23 (17)</td>
<td>0.28 (0.12-0.66)</td>
<td>0.002</td>
</tr>
<tr>
<td></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td><strong>Secondary endpoints</strong></td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Readmissions for</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Recurrent pancreatitis</td>
<td>3 (2)</td>
<td>12 (9)</td>
<td>0.27 (0.08-0.92)</td>
<td>0.02</td>
</tr>
<tr>
<td>Colics</td>
<td>2 (1)</td>
<td>7 (5)</td>
<td>0.3 (0.06-1.43)</td>
<td>0.11</td>
</tr>
<tr>
<td>Choledocholithiasis</td>
<td>1 (1)</td>
<td>2 (1)</td>
<td>0.53 (0.05-5.79)</td>
<td>0.6</td>
</tr>
<tr>
<td>Cholecystitis</td>
<td>0</td>
<td>2 (1)</td>
<td></td>
<td></td>
</tr>
<tr>
<td>Mortality</td>
<td>1 (1)</td>
<td>0</td>
<td></td>
<td>0.30</td>
</tr>
</tbody>
</table>
Anti/probiotics

- Intravenous antibiotic prophylaxis is not recommended for the prevention of infectious complications in acute pancreatitis. (GRADE 1B, strong agreement)

- Probiotic prophylaxis is not recommended for the prevention of infectious complications in acute pancreatitis. (GRADE 1B, strong agreement).
Probiotic prophylaxis: no reduction of infections

THE LANCET

Probiotic prophylaxis in predicted severe acute pancreatitis: a randomised, double-blind, placebo-controlled trial


PROPATRIA trial
Therapy
Necrotizing pancreatitis
Necrotizing pancreatitis

• 70% sterile necrosis: 6% mortality with a conservative, multidisciplinary approach\textsuperscript{1,2}

• 30% infected necrosis: 15% mortality\textsuperscript{2}

• We cannot prevent infected necrosis (yet)
  – Antibiotics
  – Probiotics
  – Early enteral nutrition

\textsuperscript{1}Buchler, Ann Surg 2000
\textsuperscript{2}Van Santvoort, Gastroenterol 2011
Indication for intervention

- Infected necrosis usually clinically obvious.
- FNA rarely needed with postponed approach
  - negative FNA: not reliable
  - positive FNA: 99% certainty of infection
- Sterile necrosis is rarely an indication for intervention in the 1st admission
Step-up approach: DDD

- **Delay**
  - Using antibiotics, until encapsulation

- **Drain**
  - Percutaneous catheter drainage (PCD)
  - Endoscopic transluminal drainage (ETD)

- **Debride**
  - Retroperitoneal percutaneous necrosectomy (MIRPN)
  - Retroperitoneal 5cm incision necrosectomy (VARD)
  - Laparoscopic transgastric necrosectomy (LTN)
  - Endoscopic transluminal necrosectomy (ETN)
  - Open necrosectomy
Let’s vote

• Is the step-up approach (drainage before necrosectomy) current ‘best practice’ for treating infected necrosis?

YES

NO

Recent survey: 87% of experts used step-up approach
Step-up approach: DDD

- **Delay**
  - Using antibiotics, until encapsulation

- **Drain**
  - Percutaneous catheter drainage (PCD)
  - Endoscopic transluminal drainage (ETD)

- **Debride**
  - Retroperitoneal percutaneous necrosectomy (MIRPN)
  - Retroperitoneal 5cm incision necrosectomy (VARD)
  - Laparoscopic transgastric necrosectomy (LTN)
  - Endoscopic transluminal necrosectomy (ETN)
  - Open necrosectomy
Minimally invasive

→ Hypothesis: less surgical stress in an already critically ill patient
Percut. catheter drainage
Syst review perc drainage

• 384 patients in 11 studies (1 RCT)
  – Preoperative organ failure: 67%
  – Infected necrosis: 71%

• Successful PCD: 55% (no debridement needed)
  – Complications: 27%
  – Mortality 17%

Van Baal et al - BJS 2011
A Step-up Approach or Open Necrosectomy for Necrotizing Pancreatitis

Hjalmar C. van Santvoort, M.D., Marc G. Besselink, M.D., Ph.D., Olaf J. Bakker, M.D., H. Sijbrand Hofker, M.D., Marja A. Boermeester, M.D., Ph.D.,

PANTER trial

Tom Karsten, M.D., Ph.D., Eric J. Hesselink, M.D., Ph.D., Cornelis J. van Laarhoven, M.D., Ph.D., Camiel Rosman, M.D., Ph.D., Koop Bosscha, M.D., Ph.D., Ralph J. de Wit, M.D., Ph.D., Alexander P. Houdijk, M.D., Ph.D., Maarten S. van Leeuwen, M.D., Ph.D., Erik Buskens, M.D., Ph.D., and Hein G. Gooszen, M.D., Ph.D.,

for the Dutch Pancreatitis Study Group*
PANTER trial: PICO

- **Patients:** 88 patients with clinical evidence of infected (peri-)pancreatic necrosis
- **Intervention:** step-up approach (delay, drain, debride)
- **Comparison:** open necrosectomy (delay, debride)
- **Outcome:** composite endpoint of major morbidity and mortality

19 Dutch hospitals, 2005-2008
PANCER trial: results 1/2

• Percutaneous catheter drainage was technically feasible in **98%** of patients

• Percutaneous catheter drainage was the only intervention needed in **35%** of patients in the step-up arm

• Step-up approach (vs primary open) decreased incidence of new multi-organ failure from **40% to 12%**
<table>
<thead>
<tr>
<th>Endpoint</th>
<th>Primary open necrosectomy (N= 45)</th>
<th>Surgical step-up approach (N= 43)</th>
<th>P</th>
</tr>
</thead>
<tbody>
<tr>
<td>Death or major morbidity</td>
<td>31 (69%)</td>
<td>17 (40%)</td>
<td>0.006</td>
</tr>
<tr>
<td>New onset multiple organ failure</td>
<td>19 (42%)</td>
<td>5 (12%)</td>
<td>0.001</td>
</tr>
<tr>
<td>Intra-abdominal bleeding</td>
<td>10 (22%)</td>
<td>7 (16%)</td>
<td>0.48</td>
</tr>
<tr>
<td>Enterocutaneous fistula/Perforation of a visceral organ</td>
<td>10 (22%)</td>
<td>6 (14%)</td>
<td>0.32</td>
</tr>
<tr>
<td>Death</td>
<td>7 (16%)</td>
<td>8 (19%)</td>
<td>0.70</td>
</tr>
</tbody>
</table>
4 pts only treated with PCD
Video-Assisted Retrop. Debridement (VARD)

Van Brunschot & DPSG – Clin Gas Hep 2011
YouTube: “VARD pancreatitis”
Endoscopic Transgastric vs Surgical Necrosectomy for Infected Necrotizing Pancreatitis
A Randomized Trial

Olaf J. Bakker, MD
Hjalmar C. van Santvoort, MD, PhD
Sandra van Brunschot, MD
Ronald B. Geskus, PhD
Marc G. Besselink, MD, PhD
Thomas L. Bollen, MD
Casper H. van Eijck, MD, PhD
Paul Fockens, MD, PhD
Eric J. Hazebroek, MD, PhD
Rian M. Nijmeijer, MD
Jan-Werner Poley, MD
Bert van Ramshorst, MD, PhD
Frank P. Vleggaar, MD, PhD
Marja A. Boermeester, MD, PhD
Hein C. Gooszen, MD, PhD
Bas L. Weusten, MD, PhD
Robin Timmer, MD, PhD
for the Dutch Pancreatitis Study Group

JAMA, March 14, 2012—Vol 307, No. 10
Corrected on March 13, 2012
Results PENGUIN trial (n=20)

Necrosectomy
- Surgery
- Transgastric endoscopy

![Graph showing interleukin 6 levels over time with indication of statistical significance: (P = .004)](image-url)
Results PENGUIN trial (2)

- Reduction of death + major complications: 80% → 20%
- Reduction new multiple organ failure: 50% → 0%
- Reduction pancreatic fistula: 70% → 10%

→ small study, not powered for clinical endpoints
Transluminal ENdoscopic step-up approach vs SurgIcal step-up apprOach in infected Necrotizing pancreatitis

Janneke van Grinsven

Paul Fockens
TENSION trial: PICO

- **Patients:** 98 patients with (suspected) infected necrosis
- **Intervention:** endoscopic step-up approach
- **Comparison:** surgical step-up approach
- **Outcome:** major complications and death

25 Dutch hospitals, 2011-2014
Take home message

1. Use the guidelines, Apps!
   - Diagnosis: lipase / amylase, CT ideally >3 days
   - Fluid infusion aimed at goals
   - ERCP in cholangitis. Pred. severe? = APEC trial!
   - Oral diet
   - Infected necrosis? Step-up approach

2. Acute (or chronic) pancreatitis?
Thank you