Acute Pancreatitis: Current aspects in Diagnosis and Treatment

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Faculdade de Ciências Médicas da Santa Casa de São Paulo
Introduction

- Acute Pancreatitis
  - Common disease
  - Incidence
    - 50-80 patients/year/100,000 inhabitants USA

Toouli et al - J Gastroenterol Hepatol, 2002
Acute pancreatitis in Brazil - 2006

Brasil: 27,077  15.9 patients/100,000 inhabitants/year
São Paulo: 1,999  19.2 patients/100,000 inhabitants/year
Introduction

Acute pancreatitis

Santa Casa:

2 patients / week

2 severe patients / month
Introduction

- Treatment of Acute Pancreatitis
  - Controversial in many topics
  - Difficulties in clinical trials
  - Small number of severe AP patients per center
**What's the best period to define severity of patients with severe acute pancreatitis?**

<table>
<thead>
<tr>
<th>Método</th>
<th>n (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Avaliação clínica</td>
<td>79 (14,8)</td>
</tr>
<tr>
<td>Critérios de Ranson</td>
<td>76 (14,3)</td>
</tr>
<tr>
<td>Avaliação clínica + Ranson + TC</td>
<td>57 (10,7)</td>
</tr>
<tr>
<td>APACHE II</td>
<td>39 (7,3)</td>
</tr>
<tr>
<td>Avaliação clínica + APACHE II + TC + PCR</td>
<td>13 (3,0)</td>
</tr>
<tr>
<td>Enteral</td>
<td>26.7%</td>
</tr>
<tr>
<td>Parenteral</td>
<td>46.6%</td>
</tr>
<tr>
<td>Enteral + Parenteral</td>
<td>26.7%</td>
</tr>
<tr>
<td>Após 21 dias</td>
<td>22.6%</td>
</tr>
<tr>
<td>116</td>
<td>116</td>
</tr>
</tbody>
</table>

**De Campos et al. Rev Col Bras Cir, 2008 / DDW 2008 - San Diego, CA**
Topics to discuss

- How to confirm the diagnosis
- How to determine severity
- How to determine etiology
- How to treat these patients
  - Antibiotics
  - Nutrition
  - ERCP
  - Surgical treatment
Topics to discuss

- How to confirm the diagnosis
- How to determine severity
- How to determine etiology
- How to treat these patients
  - Antibiotics
  - Nutrition
  - ERCP
  - Surgical treatment
Diagnosis

Current definition

- Clinical presentation
- AMILASE / LIPASE > 3x
- CT (ultrasound / MR)

2 out of 3 = acute pancreatitis

Banks PA & Freeman ML - Am J Gastroenterol, 2006
Topics to discuss

- How to confirm the diagnosis
- How to determine severity
- How to determine etiology
- How to treat these patients
  - Antibiotics
  - Nutrition
  - ERCP
  - Surgical treatment
Severity

- Death in acute pancreatitis

1-2nd week

SIRS
Organic failure

X

after 2nd week

Necrosis + Infection

Schmidt et al, Gut 1999
Toouli et al - J Gastroenterol Hepatol, 2002
Clancy et al - J Gastrointest Surg, 2005
Severity

- 2 factors determine the prognosis of a patient with acute pancreatitis

Organic failure  Necrosis/Infection

Classifications of severity

Toouli et al - J Gastroenterol Hepatol, 2002
Werner – Pancreatology, 2003
Clancy et al - J Gastrointest Surg, 2005
Classification of Acute Pancreatitis

- Marselha Meeting 1963
- Marselha Meeting 2 1984
- Atlanta Meeting 1992
Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus

Peter A Banks,1 Thomas L Bollen,2 Christos Dervenis,3 Hein G Gooszen,4 Colin D Johnson,5 Michael G Sarr,6 Gregory G Tsiftos,7 Santhi Swaroop Vege8
Acute Pancreatitis Classification Working Group

Box 3 Grades of severity

- Mild acute pancreatitis
  - No organ failure
  - No local or systemic complications

- Moderately severe acute pancreatitis
  - Organ failure that resolves within 48 h (transient organ failure) and/or
  - Local or systemic complications without persistent organ failure

- Severe acute pancreatitis
  - Persistent organ failure (>48 h)
    - Single organ failure
    - Multiple organ failure
Classification of the Severity of Acute Pancreatitis: How Many Categories Make Sense?

Maxim S. Petrov, MD, MPH* and John A. Windsor, MBChB, MD, FRACS†

There is an ongoing effort to revise the 1992 Atlanta classification of acute pancreatitis in the light of emerging evidence. The categorization of the severity of acute pancreatitis is one of the key elements of the classification. This paper aims to define the optimal number of categories and provide their definitions on sound clinical grounds.


### Table 1. Classification and definitions of four categories for the severity of acute pancreatitis

<table>
<thead>
<tr>
<th>Severity category</th>
<th>Local complications</th>
<th>Systemic complications</th>
</tr>
</thead>
<tbody>
<tr>
<td>Mild</td>
<td>No (peri)pancreatic complication</td>
<td>and</td>
</tr>
<tr>
<td>Moderate</td>
<td>Sterile (peri)pancreatic complication</td>
<td>or</td>
</tr>
<tr>
<td>Severe</td>
<td>Infectious (peri)pancreatic complication</td>
<td>or</td>
</tr>
<tr>
<td>Critical</td>
<td>Infectious (peri)pancreatic complication</td>
<td>and</td>
</tr>
</tbody>
</table>

*Severity is graded on the basis of more severe local or systemic complication (e.g., sterile pancreatic necrosis without organ failure has to be graded as “moderate”; sterile pancreatic necrosis with persistent organ failure has to be graded as “severe”).
Severity evaluation

Phase 1 - SIRS and Organic failure

Box 2: Signs of Systemic Inflammatory Response Syndrome (SIRS)

- Heart rate > 90 beats/min
- Core temperature < 36°C or > 38°C
- White blood count < 4000 or > 12000/mm³
- Respirations > 20/min or PCO₂ < 32 mm Hg

DDW 2008
Severity evaluation

Phase 1 - SIRS and Organic failure

<table>
<thead>
<tr>
<th>Table 1</th>
<th>Modified Marshall scoring system for organ dysfunction</th>
</tr>
</thead>
<tbody>
<tr>
<td><strong>Organ system</strong></td>
<td><strong>Score</strong></td>
</tr>
<tr>
<td>Respiratory ($P_{aO_2}/FiO_2$)</td>
<td>$&gt; 400$</td>
</tr>
<tr>
<td>Renal*</td>
<td>Serum creatinine, µmol/L</td>
</tr>
<tr>
<td></td>
<td>Serum creatinine, mg/dL</td>
</tr>
<tr>
<td>Cardiovascular (systolic blood pressure, mm Hg)</td>
<td>$&gt; 90$</td>
</tr>
<tr>
<td>For non-ventilated patients, the FiO$_2$ can be estimated from below</td>
<td><strong>Supplemental oxygen (l/min)</strong></td>
</tr>
</tbody>
</table>

A score of 2 or more in any system defines the presence of organ failure.

* A score for patients with pre-existing chronic renal failure depends on the extent of further deterioration of baseline renal function. No formal correction exists for a baseline serum creatinine $\geq 134$ µmol/L or $\geq 1.4$ mg/dL.

† Definitive inotropic support.
Local evaluation

Phase 2 - Necrosis and Infection

Necrosis

C Reactive Protein    CT scan
Local evaluation

Phase 2 - Necrosis and Infection

CRP - 48 hours
> 150 mg/L
Accuracy 85% for necrosis
Local evaluation

Phase 2 - Necrosis and Infection

TC – gold standard / not before 72 hs

- Peritonitis / Abdominal distention
- APACHE II ≥ 8 / SIRS / Marshall ≥ 2 / SOFA ≥ 3
- US with peripancreatic fluid or pancreatic alterations
- CRP > 150 mg/L
- Not improving / worse / difficult to feed
- Need to confirm diagnosis
Local severity

Tomographic Classification
(Balthazar-Ranson – Tomographic severity index)

Phase 2 - Necrosis and Infection

TOTAL = 0 - 10
Local complications

- Interstitial edematous pancreatitis
- Necrotising pancreatitis (pancreatic / peripancreatic necrosis)
- Acute peripancreatic fluid collection
- Acute necrotic collection
- Pancreatic pseudocyst
- Walled-off necrosis

Early phase

Late phase
Local complications

Interstitial edematous pancreatitis
Local complications

Peripancreatic necrosis
Pancreatic necrosis

Local complications

Pancreatic necrosis
Acute peripancreatic fluid collection

Local complications

Acute peripancreatic fluid collection
Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus

Local complications

Acute necrotic collection
Practical aspects

Assess

- Systemic complications
- Local complications
Practical aspects

How to assess Systemic complications?

- Ranson
- Glasgow
- SIRS
- Apache II
- SOFA
- Marshall

Repeat in 48 hs
(not possible to Ranson and Glasgow)
Practical aspects

How to assess Local complications

- C Reactive protein
- Computed tomography
Practical aspects

How we do at Santa Casa?

Systemic complications

- SIRS
- Apache II
- SOFA
- Marshall

Repeated in 48 hs and when necessary

Patients with severe disease have daily scores
Aspectos Práticos

How we do at Santa Casa
Local complications

-C Reactive Protein - 48 hs
-CT 72-96 hs after the onset of symptoms in selected patients
Topics to discuss

- How to confirm the diagnosis
- How to determine severity
- How to determine etiology
- How to treat these patients
  - Antibiotics
  - Nutrition
  - ERCP
  - Surgical treatment
Etiologia

- Biliar: 50,0%
- Álcool: 34,8%
- Biliar + Álcool: 8,3%
- Idiopático: 6,1%
- Hipertigliceridemia: 0,8%

Serviço de Emergência – FCM Santa Casa SP
Etiology

- Laboratory tests - up to 24 hours
  - Calcium
  - Triglycerides
  - Medicines
  - Previous diseases

UK guidelines for the management of acute pancreatitis - Gut, 2005
Banks PA & Freeman ML - Am J Gastroenterol, 2006
Etiology

Ultrasound

- All patients with acute pancreatitis
- 2nd US if the 1st was negative and there is no obvious cause
- Endoscopic ultrasound if the 1st and the 2nd were negatives and there is no other cause

Banks PA & Freeman ML - Am J Gastroenterol, 2006

UK guidelines for the management of acute pancreatitis - Gut, 2005
Etiology

Idiopathic pancreatitis

Excluir

- Biliary
  - 65-85% of patients
- Alcohol
- Dyslipidemia
- Biliary cystic disease
- Pancreas Divisum
- Chronic pancreatitis
  - autoimmune 5-6%
- Duodenal obstruction
- Medicines

Pancreatic neoplasms

- 3% < 40 y/o / 25% > 60 y/o
- Toxins
  - insecticides / scorpions
- Trauma
- Vasculitis
- Infections
  - virus / ascaris
- Celiac disease
- Genetic (PRSS1 / CFTR / SPINK-1)

Guda & Forsmark, 2008
Topics to discuss

- How to confirm the diagnosis
- How to determine severity
- How to determine etiology
- How to treat these patients
  - Antibiotics
  - Nutrition
  - ERCP
  - Surgical treatment
There is no specific treatment :(
Topics to discuss

- How to confirm the diagnosis
- How to determine severity
- How to determine etiology
- How to treat these patients
  - Antibiotics
  - Nutrition
  - ERCP
  - Surgical treatment
Antibiotics

Mild acute pancreatitis
   No place
   Rare (cholangitis)

Severe acute pancreatitis
   Therapeutic
   “Prophylactic”

A lot of doubts and discussions
antibiotics in acute pancreatitis
Lack of evidence

X

Group of patients with benefits

- USA
  - ACS / SSAT: do no recommend
  - AGA: split

- Europe
  - UK / Netherlands: do no recommend
  - Germany / Italy: use

- Asia / South Africa / South America: use
“Although we know that a group of patients benefits from the use of prophylactic antibiotics, studies fail to prove this benefit.”

Hjalmar van Santvoort, M.D
Acute pancreatitis study group
“I use prophylactic antibiotics in patients with severe acute pancreatitis with necrosis > 30% because I see their benefit, despite Michael Sarr get mad at me”
Prophylactic Antibiotics Reduce Pancreatic Necrosis in Acute Necrotizing Pancreatitis: A Meta-Analysis of Randomized Trials

Linhua Yao  Xiayue Huang  Yuqin Li  Ruihua Shi  Guoxin Zhang

Reduction in pancreatic necrosis
Conclusion: The current evidence does not support the use of prophylactic antibiotics as routine in severe acute pancreatitis, but further studies may show that a sub-population can benefit from its use.
Current position about the use of antibiotics in acute pancreatitis

- There is no definitive conclusion
- Probably there won’t be a definitive conclusion
- Each hospital have to determine its policy
  - “On demand” X Routine
- No study has shown that the use of antibiotics impairs the evolution of these patients
1- Should we use prophylactic antibiotics?

Yes (personal opinion). There is no agreement.

2- In which patient?

Pancreatic necrosis > 30%

When there is the diagnosis of necrosis

3- How to use it?

a) Which one?

IMIPENEM or CIPROFLOXACIN + METRONIDAZOL

b) How long?

10 – 14 days
Topics to discuss

- How to confirm the diagnosis
- How to determine severity
- How to determine etiology
- How to treat these patients
  - Antibiotics
  - Nutrition
  - ERCP
  - Surgical treatment
Enteral nutritional support should be used as first choice.

- The evidence is not conclusive to support the use of enteral nutrition in all patients with severe acute pancreatitis. However, if nutritional support is required, the enteral route should be used if that can be tolerated (grade A). The nasogastric route for feeding can be used as it appears to be effective in 80% of cases (grade B).
Current Management of Acute Pancreatitis

Thomas E. Clancy, M.D., Eric P. Benoit, M.D., Stanley W. Ashley, M.D.

- Journal of Gastrointestinal Surgery Vol. 9, No. 3, 2005

Parenteral nutrition has not shown advantages in any study

Enteral nutrition
- Lower septic complications
- Reduction in organ failure
- Reduction in CRP
- Shorter hospital stay

Table 1. Controlled trials of nutritional support in patients with acute pancreatitis

<table>
<thead>
<tr>
<th>Study</th>
<th>Glasgow Coma Scale score</th>
<th>Parenteral nutrition</th>
<th>Change in inflammatory mediators</th>
<th>Nonsignificant trend to improved lymphocyte proliferation and interleukin 8 release in glutamine group</th>
</tr>
</thead>
<tbody>
<tr>
<td>de Beaux et al. (1998)</td>
<td>⩾3</td>
<td>conventional versus glutamine enhanced</td>
<td></td>
<td></td>
</tr>
</tbody>
</table>
Prevention of infection

**Enteral Nutrition and the Risk of Mortality and Infectious Complications in Patients With Severe Acute Pancreatitis**

_A Meta-analysis of Randomized Trials_  

Maxim S. Petrov, MD; Hjalmar C. van Santvoort, MD; Marc G. H. Besselink, MD; Geert J. M. G. van der Heijden, PhD; John A. Windsor, MD, FRACS; Hein G. Gooszen, MD, PhD

<table>
<thead>
<tr>
<th>Source</th>
<th>Year</th>
<th>EN Group</th>
<th>PN Group</th>
<th>Forest Plot – RR (IV+)</th>
<th>Weight, %</th>
<th>Association Measure (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kallamertzos et al⁹⁹</td>
<td>1997</td>
<td>5/15</td>
<td>10/20</td>
<td>6.36</td>
<td>100</td>
<td>0.506 (0.234-1.315)</td>
</tr>
<tr>
<td>Gupta et al¹⁰</td>
<td>2003</td>
<td>1/6</td>
<td>2/9</td>
<td>4.90</td>
<td></td>
<td>0.565 (0.262-1.094)</td>
</tr>
<tr>
<td>Louie et al¹¹</td>
<td>2005</td>
<td>5/10</td>
<td>7/18</td>
<td>6.36</td>
<td></td>
<td>0.257 (0.027-1.434)</td>
</tr>
<tr>
<td>Eckerwall et al¹²</td>
<td>2005</td>
<td>5/23</td>
<td>0/25</td>
<td>2.90</td>
<td></td>
<td>7.563 (0.413-133.315)</td>
</tr>
<tr>
<td>Petrov et al¹¹</td>
<td>2005</td>
<td>11/35</td>
<td>21/34</td>
<td>58.50</td>
<td></td>
<td>0.395 (0.236-0.665)</td>
</tr>
<tr>
<td>Meta-analysis</td>
<td>2005</td>
<td>41/40</td>
<td>46/106</td>
<td></td>
<td>100</td>
<td>0.468 (0.265-0.769)</td>
</tr>
</tbody>
</table>

**Figure 2.** Forest plot for total infectious complications. CI indicates confidence interval; EN, enteral nutrition; IV, inverse variance; PN, parenteral nutrition; and RR, relative risk.

<table>
<thead>
<tr>
<th>Source</th>
<th>Year</th>
<th>EN Group</th>
<th>PN Group</th>
<th>Forest Plot – RR (IV+)</th>
<th>Weight, %</th>
<th>Association Measure (95% CI)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Kallamertzos et al⁹⁹</td>
<td>1997</td>
<td>1/18</td>
<td>2/20</td>
<td>12.00</td>
<td>100</td>
<td>0.555 (0.055-5.622)</td>
</tr>
<tr>
<td>Louie et al¹¹</td>
<td>2005</td>
<td>0/10</td>
<td>3/16</td>
<td>14.40</td>
<td></td>
<td>0.247 (0.014-4.546)</td>
</tr>
<tr>
<td>Eckerwall et al¹²</td>
<td>2005</td>
<td>1/23</td>
<td>0/25</td>
<td>12.00</td>
<td></td>
<td>3.25 (0.126-75.006)</td>
</tr>
<tr>
<td>Petrov et al¹¹</td>
<td>2005</td>
<td>2/39</td>
<td>12/24</td>
<td>32.00</td>
<td></td>
<td>0.162 (0.039-0.67)</td>
</tr>
<tr>
<td>Meta-analysis</td>
<td>2005</td>
<td>4/85</td>
<td>17/67</td>
<td></td>
<td>100</td>
<td>0.322 (0.106-0.98)</td>
</tr>
</tbody>
</table>

**Figure 3.** Forest plot for mortality. CI indicates confidence interval; EN, enteral nutrition; IV, inverse variance; PN, parenteral nutrition; and RR, relative risk.
Nutrition in Acute Pancreatitis

- **Parenteral nutrition**
  - It does not stimulate pancreatic secretion
  - Infections complications
  - Procedure complications
  - High cost

- **Enteral nutrition**
  - REDUCTION OF BACTERIAL TRANSLOCATION
  - Physiologic
  - Lower cost
  - Some stimulus in pancreatic secretion
  - Needs to be placed by endoscopy or radioscopy
Nutrition in Acute Pancreatitis

Parenteral nutrition × Enteral nutrition

Enteral nutrition

Tube placed in the jejunum
Nutrition in Acute Pancreatitis

- **Current position** *(nutrition within 48 hours)*
  - Enteral nutrition is preferred
  - No vomits, distention or significant pain
    - Oral diet - liquid with low-fat
    - Nasojejunalostomy tube
      - start with 20 ml/h semi-elemental diet
      - progression 10 ml/h/day
  - Parenteral if significant intolerance *(rare)*
  - Keep enteral nutrition in small volume
Topics to discuss

- How to confirm the diagnosis
- How to determine severity
- How to determine etiology
- How to treat these patients
  - Antibiotics
  - Nutrition
  - ERCP
  - Surgical treatment
Severe acute pancreatitis x ERCP

IAP Guidelines for the Surgical Management of Acute Pancreatitis

Waldemar Uhl\textsuperscript{a} Andrew Warshaw\textsuperscript{b} Clement Imrie\textsuperscript{c} Claudio Bassi\textsuperscript{d} Colin J. McKay\textsuperscript{e} Paul G. Lankisch\textsuperscript{e} Ross Carter\textsuperscript{e} Eugene Di Magno\textsuperscript{f} Peter A. Banks\textsuperscript{g} David C. Whitcomb\textsuperscript{h} Christos Dervenis\textsuperscript{i} Charles D. Ulrich\textsuperscript{j} Kat Satake\textsuperscript{k} Paula Ghaneh\textsuperscript{l} Werner Hartwig\textsuperscript{a} Jens Werner\textsuperscript{a} Gerry McEntee\textsuperscript{m} John P. Neoptolemos\textsuperscript{i} Markus W. Büchler\textsuperscript{a}

Cochrane Review, 2004
Ayub K, Imada R, Slavin J

Given the lack of a clear consensus on this subject, no recommendation can be made on the use of ERCP and ES in severe gallstone-associated acute pancreatitis per se, although all are agreed that ERCP and ES are indicated in the presence of obstructive jaundice and/or acute cholangitis.
Early Endoscopic Retrograde Cholangiopancreatography in Predicted Severe Acute Biliary Pancreatitis

A Prospective Multicenter Study

Hjalmar C. van Santvoort, MD,* Marc G. Besselink, MD, PhD,* Annemarie C. de Vries, MD,† Marja A. Boermeester, MD, PhD,‡ Kathelijn Fischer, MD, PhD,§ Thomas L. Bollen, MD,¶ Geert A. Cirkel, MD,* Alexander F. SchaapHerder, MD, PhD,‖ Vincent B. Nieuwenhuijs, MD, PhD,** Harry van Goor, MD, PhD,†† Cees H. Dejong, MD, PhD,†† Casper H. van Eijck, MD, PhD,§§ Ben J. Witteman, MD, PhD,¶¶ Bas L. Weusten, MD, PhD,¶¶¶ Cees J. van Laarhoven, MD, PhD,*** Peter J. Wahab, MD, PhD,††† Adriaan C. Tan, MD, PhD,††† Mathijs P. Schwartz, MD, PhD,§§§ Erwin van der Harst, MD, PhD,§§§ Miguel A. Cuesta, MD, PhD,¶¶¶¶ Peter D. Siersema, MD, PhD,**** Hein G. Gooszen, MD, PhD,* Karel J. van Erpecum, MD, PhD,**** and the members of the Dutch Acute Pancreatitis Study Group

Annals of Surgery • Volume 250, Number 1, July 2009

<table>
<thead>
<tr>
<th>TABLE 2. Outcome of 153 Patients With Predicted Severe Acute Biliary Pancreatitis Undergoing Early ERCP or Conservative Treatment</th>
</tr>
</thead>
<tbody>
<tr>
<td>Characteristics</td>
</tr>
<tr>
<td></td>
</tr>
<tr>
<td>Primary endpoints</td>
</tr>
<tr>
<td>Overall complications</td>
</tr>
<tr>
<td>Pancreatic necrosis</td>
</tr>
<tr>
<td>&lt;30% pancreatic necrosis</td>
</tr>
<tr>
<td>&gt;30% pancreatic necrosis</td>
</tr>
<tr>
<td>Infected pancreatic necrosis</td>
</tr>
<tr>
<td>Bacteremia</td>
</tr>
<tr>
<td>Infected ascites</td>
</tr>
<tr>
<td>Pneumonia</td>
</tr>
<tr>
<td>New onset organ failure</td>
</tr>
<tr>
<td>New onset multi-organ failure</td>
</tr>
<tr>
<td>Bowel ischaemia*</td>
</tr>
<tr>
<td>Mortality</td>
</tr>
<tr>
<td>Secondary endpoints</td>
</tr>
<tr>
<td>CTSI†</td>
</tr>
<tr>
<td>Percutaneous drainage</td>
</tr>
<tr>
<td>Operative necrosectomy</td>
</tr>
<tr>
<td>Intensive care admission</td>
</tr>
<tr>
<td>Total intensive care stay in days</td>
</tr>
<tr>
<td>Total hospital stay in days</td>
</tr>
</tbody>
</table>
Severe Acute Pancreatitis x ERCP

Current position

ERCP

- Cholangitis (jaundice + Biliary dilation + fever > 38.5°C / leukocytosis > 18,000)
- Calculus impacted in the papilla
  - *bilirubin curve (> 2.5)
- Before cholecystectomy
  - *if predictive factors of choledocholithiasis
Topics to discuss

- How to confirm the diagnosis
- How to determine severity
- How to determine etiology
- How to treat these patients
  - Antibiotics
  - Nutrition
  - ERCP
  - Surgical treatment
Tratamento Cirúrgico

• INFECTION = SURGERY

<5% patients
Questões

- How to make the diagnosis of infection?
- How to decide by the surgical treatment?
- How to operate?
Diagnosis of Infection

- Clinical
- Laboratory
- * Procalcitonin / CRP
- Computed Tomography
- Fine needle aspiration (gold standard)

"Important the diagnosis at the right time, but not necessarily very early"

Diagnosis of Infection

- Clinical
  - Patient at risk (extensive necrosis)
  - Probable time (from the 2nd week)
- Worsening
  - New organ failure
  - worsening of organ failure already diagnosed
○ Study in 5 centers with 104 patients
○ Procalcitonin 3-4 days after AP
○ \( \geq 3.5 \text{ ng / ml} \) on 2 consecutive days
  ○ Sensitivity 93% specificity 88%
  ○ Pancreatic infection with organ failure
Early Assessment of Pancreatic Infections and Overall Prognosis in Severe Acute Pancreatitis by Procalcitonin (PCT)

A Prospective International Multicenter Study

Bettina M. Rau, MD,* Esko A. Kemppainen, MD,‡ Andrew A. Gumbs, MD,§ Markus W. Büchler, MD,∥ Karl Wegscheider, PhD,¶ Claudio Bassi, MD,§ Pauli A. Puolakkainen, MD,¶ and Hans G. Beger, MD, FACS†

<table>
<thead>
<tr>
<th>Cutoff</th>
<th>Sensitivity (%)</th>
<th>Specificity (%)</th>
<th>PPV (%)</th>
<th>NPV (%)</th>
</tr>
</thead>
<tbody>
<tr>
<td>Infected necrosis</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCT (ng/mL)</td>
<td>≥4.0</td>
<td>65</td>
<td>89</td>
<td>52</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>≥390</td>
<td>41</td>
<td>92</td>
<td>50</td>
</tr>
<tr>
<td>Infected necrosis + MODS</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCT (ng/mL)</td>
<td>≥5.6</td>
<td>90</td>
<td>89</td>
<td>47</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>≥430</td>
<td>50</td>
<td>99</td>
<td>83</td>
</tr>
<tr>
<td>Death</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCT (ng/mL)</td>
<td>≥3.5</td>
<td>100</td>
<td>82</td>
<td>32</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>≥310</td>
<td>63</td>
<td>67</td>
<td>14</td>
</tr>
<tr>
<td>Infected necrosis + MODS or death</td>
<td></td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>PCT (ng/mL)</td>
<td>≥3.5</td>
<td>93</td>
<td>88</td>
<td>56</td>
</tr>
<tr>
<td>CRP (mg/L)</td>
<td>≥430</td>
<td>40</td>
<td>100</td>
<td>100</td>
</tr>
</tbody>
</table>

Analysis was based on the highest PCT and CRP value, which was reached on at least 2 consecutive days within the total observation period. Infected necrosis: AUC PCT vs. CRP: *P = NS*. Infected necrosis + MODS: AUC PCT vs. CRP: *P = NS*. Death: AUC PCT vs. CRP: *P < 0.002*. Infected necrosis + MODS and death: AUC PCT vs. CRP: *P < 0.01*.

NS indicates not significant.
Computed Tomography

- Gas: 30-50%
Fine-needle aspiration

- Gold-standard (1980’s)
- Guided by CT or US
  - Gram / Culture
- False-negative: 20-50%!!!!

Questões

- How to make the diagnosis of infection?
- How to decide by the surgical treatment?
- How to operate?
IAP Guidelines for the Surgical Management of Acute Pancreatitis

Waldemar Uhl\textsuperscript{a}, Andrew Warshaw\textsuperscript{b}, Clement Imrie\textsuperscript{c}, Claudio Bassi\textsuperscript{d}, Colin J. McKay\textsuperscript{c}, Paul G. Lankisch\textsuperscript{a}, Ross Carter\textsuperscript{c}, Eugene Di Magno\textsuperscript{f}, Peter A. Banks\textsuperscript{g}, David C. Whitcomb\textsuperscript{h}, Christos Dervenis\textsuperscript{i}, Charles D. Ulrich\textsuperscript{j}, Kat Satake\textsuperscript{k}, Paula Ghanei\textsuperscript{l}, Werner Hartwig\textsuperscript{a}, Jens Werner\textsuperscript{a}, Gerry McEntee\textsuperscript{m}, John P. Neoptolemos\textsuperscript{l}, Markus W. Buchler\textsuperscript{a}

Recommendation 4: Infected pancreatic necrosis in patients with clinical signs and symptoms of sepsis is an indication for intervention including surgery and radiological drainage (recommendation grade B).

5 Patients with sterile pancreatic necrosis (FNAB negative) should be managed conservatively and only undergo intervention in selected cases (recommendation grade B).

Recommendation 6: Early surgery within 14 days after onset of the disease is not recommended in patients with necrotizing pancreatitis unless there are specific indications (recommendation grade B).
Surgical treatment

Early versus late necrosectomy in severe necrotizing pancreatitis


36 patients with severe acute pancreatitis

- **Group A (n=25)**
  - Necrosectomy 48-72 hours
  - Mortality 58%

- **Group B (n=11)**
  - Necrosectomy after 12 days
  - Mortality 27%

- Results with no significance
- Odds ratio for mortality: 3.4x greater in Group A
- Study discontinued due to high mortality in Group A
Surgical Treatment

- Late surgery (after 2 weeks)
- Reduces risk of bleeding
- Removal of small tissue viable
- Reduces endocrine and exocrine insufficiency
Treatment of infected necrosis

- Time of intervention
  - Great tendency to be delayed
  - Pancreatic necrosis and peri-pancreatic tends to delimit in 3-4 weeks, which facilitates the procedure
  - The impact of an additional immune stress in an initial stage can be critical to the evolution of the patient
  - Average time for intervention now: 26-33 days

It is possible to treat clinically a patient with infected necrosis?

INFECTION = SURGERY???
Severe Acute Pancreatitis: Nonsurgical Treatment of Infected Necroses

Michael Runzi, MD,* Wolfgang Niebel, MD,† Harald Goebell, MD,* Guido Gerken, MD,* and Peter Layer, MD, PhD‡

Pancreas • Volume 30, Number 3, April 2005
Severe Acute Pancreatitis: Nonsurgical Treatment of Infected Necroses

Michael Runzi, MD,* Wolfgang Niebel, MD,† Harald Goebell, MD,* Guido Gerken, MD,* and Peter Layer, MD, PhD‡

Mortality

Clinical treatment 12.5% x 20% Surgical treatment
Infected Pancreatic Necrosis and Peripancreatic Fluid Collections: Serendipitous Response to Antibiotics and Medical Therapy in Three Patients

Howard Dubner, William Steinberg, *Michael Hill, †Claudio Bassi, ‡Rashmae Chardavoyne, and §Simmy Bank
In conclusion, conservative management is effective in patients with infected pancreatic necrosis when their clinical condition is stable and/or transient end organ dysfunction is shown by a lower APACHE score at ICU. Well-designed prospective studies are needed to throw more light on this issue and can give guidelines in the appropriate selection of patients with infected pancreatic necrosis for conservative management.
Nonsurgical Treatment of Infected Pancreatic Necrosis: A Falling Myth or a Still Impassable Frontier?

Generoso Uomo

The message of the present study is that intensive nonsurgical treatment is very effective and safe in acute necrotizing pancreatitis and it should also be considered as an initial treatment modality for patients with infected necrosis. Avoiding or delaying surgery in this critically-ill group of patients opens a new and favorable frontier in clinical practice.

"... nihil aequae sanitatem impedit quam remediorum crebra mutatio; ..."
L. Annaei Senecae Epistularum Moralium ad Lucilium.
(Liber Primus; Epistula II: Seneca Lucilio Suo Salutem)

"... frequently changing the therapy is the major drawback to healing; ..."
Lucius Annaeus Seneca (Seneca the Younger, ca. 4 BC - AD 65)
The Efficacy of Nonsurgical Treatment of Infected Pancreatic Necrosis

Jun Kyu Lee, MD,* Kyeong Keun Kwak, MD,† Joo Kyung Park, MD,† Won Jae Yoon, MD,† Sang Hyub Lee, MD,† Ji Kon Ryu, MD, PhD,† Yong-Tae Kim, MD, PhD,† and Yong Bum Yoon, MD, PhD†

Pancreas • Volume 34, Number 4, May 2007

*: endoscopic drainage
†: percutaneous drainage
The pancreatic infection is indicative of immediate surgical treatment in Severe Acute Pancreatitis?

- Avoid early surgery (before 14 days)
- Pancreatic infection without organ failure consider nonoperative treatment
- Pancreatic infection with organ failure consider nonoperative treatment if up to 14 days of evolution
Early operation

- Bowel complications
  - Necrosis / perforation
- Hemorrhagic complications
  - fail in arteriography and embolisation
Questões

- How to make the diagnosis of infection?
- How to decide by the surgical treatment?
- How to operate?
Surgical treatment

- How to operate?
  - Drain collections
  - Necrosectomy
### Table 3

#### Treatment modalities for necrotizing pancreatitis

<table>
<thead>
<tr>
<th>Technique</th>
<th>Patients (n)</th>
<th>Fistulas (pancreatic/enteric)</th>
<th>Haemorrhage</th>
</tr>
</thead>
<tbody>
<tr>
<td>&quot;Open packing&quot;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Bradley 1993(^{13})</td>
<td>71</td>
<td>46%</td>
<td>7%</td>
</tr>
<tr>
<td>Branum 1998(^{13})</td>
<td>50</td>
<td>88% (72%/16%)</td>
<td>–</td>
</tr>
<tr>
<td>Bosscha 1998(^{50})</td>
<td>28</td>
<td>25%</td>
<td>50%</td>
</tr>
<tr>
<td>&quot;Planned re-laparotomies&quot;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Sarr 1991(^{47})</td>
<td>23</td>
<td>(26%/52%)</td>
<td>26%</td>
</tr>
<tr>
<td>Tsiotos 1998(^{20})</td>
<td>72</td>
<td>(19%/27%)</td>
<td>18%</td>
</tr>
<tr>
<td>&quot;Closed packing&quot;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Fernandez-del C 1998(^{19})</td>
<td>64</td>
<td>(53%/16%)</td>
<td>3%</td>
</tr>
<tr>
<td>&quot;Closed Continuous Lavage&quot;</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Farkas 1996(^{55})</td>
<td>123</td>
<td>(13%/1%)</td>
<td>2%</td>
</tr>
<tr>
<td>Büchler 2001</td>
<td>42</td>
<td>19%</td>
<td>5%</td>
</tr>
<tr>
<td>Percutaneous drainage + peritoneal lavage</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Percutaneous necrosectomy + sinus tract debridement(^{153})</td>
<td></td>
<td></td>
<td></td>
</tr>
<tr>
<td>Endoscopic(^{154})</td>
<td></td>
<td></td>
<td></td>
</tr>
</tbody>
</table>

---

Surgical treatment
Surgical treatment
Surgical Treatment
Minimally invasive treatment

- Transparietal
- Laparoscopic
- Endoscopy
- Retroperitoneal necrosectomy
Conclusion

- Confirm the diagnosis
- Severity assessment
- Look for the cause
- No specific treatment / Gallbladder stays at the hospital
- Antibiotic in necrotizing pancreatitis is controversial
- Enteral nutrition!
- ERCP in cholangitis
- Surgical treatment
  - Infection + organ failure
  - Late is better
- Step-up approach
Obrigado!

tercio@uol.com.br