

# Prise en charge des pancréatites aigües sévères

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Université Pierre et Marie-Curie-Paris6

- Pas de lien d'intérêt en lien avec cette présentation

## PANCREATITE OEDEMATEUSE

*Interstitial oedematous pancreatitis*

**Epanchement liquidien  
péripancréatique**

Résolution spontanée fréquente en  
1 semaine



**4 semaines**

## Pseudokystes

- . Résolution spontanée 50%
- . Hémorragie 10%
- . Infection 10%
- . Autre complication

## PANCREATITE NECROSANTE

*Necrotizing pancreatitis*

**Collections nécrotiques aiguës**

20 % des PA  
Morbidity et mortalité ↑

**Nécrose pancréatite collectée**

# Apprécier la gravité

=> Prédire la sévérité

⇒ Identifier les patients à risque de complications / d'évolution complexe

⇒ Scores clinico-bio-radiologiques

# Apprécier la gravité

=> Prédire la sévérité

⇒ Identifier les patients à risque de complications / d'évolution complexe

⇒ Scores clinico-bio-radiologiques

- « La maladie des scores »
  - Ranson
  - Imrie
  - CTSI
  - Balthazare
  - SOFA
  - APACHE II
  - BISAP....
- ...et des biomarqueurs (CRP, PCT...)

# Apprécier la gravité

## Hémodynamique

- PAS <90 mm Hg malgré expansion volémique adéquat ou utilisation de catécholamines

## Rénale

- Créatinémie >177  $\mu\text{mol/litre}$  après réhydratation ou besoin d'épuration extrarénal

## Respiratoire

- PaO<sub>2</sub> <60 mm Hg malgré FIO<sub>2</sub> of 0.30 Ou ventilation artificielle

*Bradley EL III. A clinically based classification system for acute pancreatitis: summary of the International Symposium on Acute Pancreatitis, Atlanta, GA, 1992. Arch Surg*

# Classification of acute pancreatitis—2012: revision of the Atlanta classification and definitions by international consensus

Peter A Banks,<sup>1</sup> Thomas L Bollen,<sup>2</sup> Christos Dervenis,<sup>3</sup> Hein G Gooszen,<sup>4</sup>  
Colin D Johnson,<sup>5</sup> Michael G Sarr,<sup>6</sup> Gregory G Tsiotos,<sup>7</sup> Santhi Swaroop Vege,<sup>8</sup>  
Acute Pancreatitis Classification Working Group

## 3 degrés de sévérité

- ▶ **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

# Apprécier la gravité

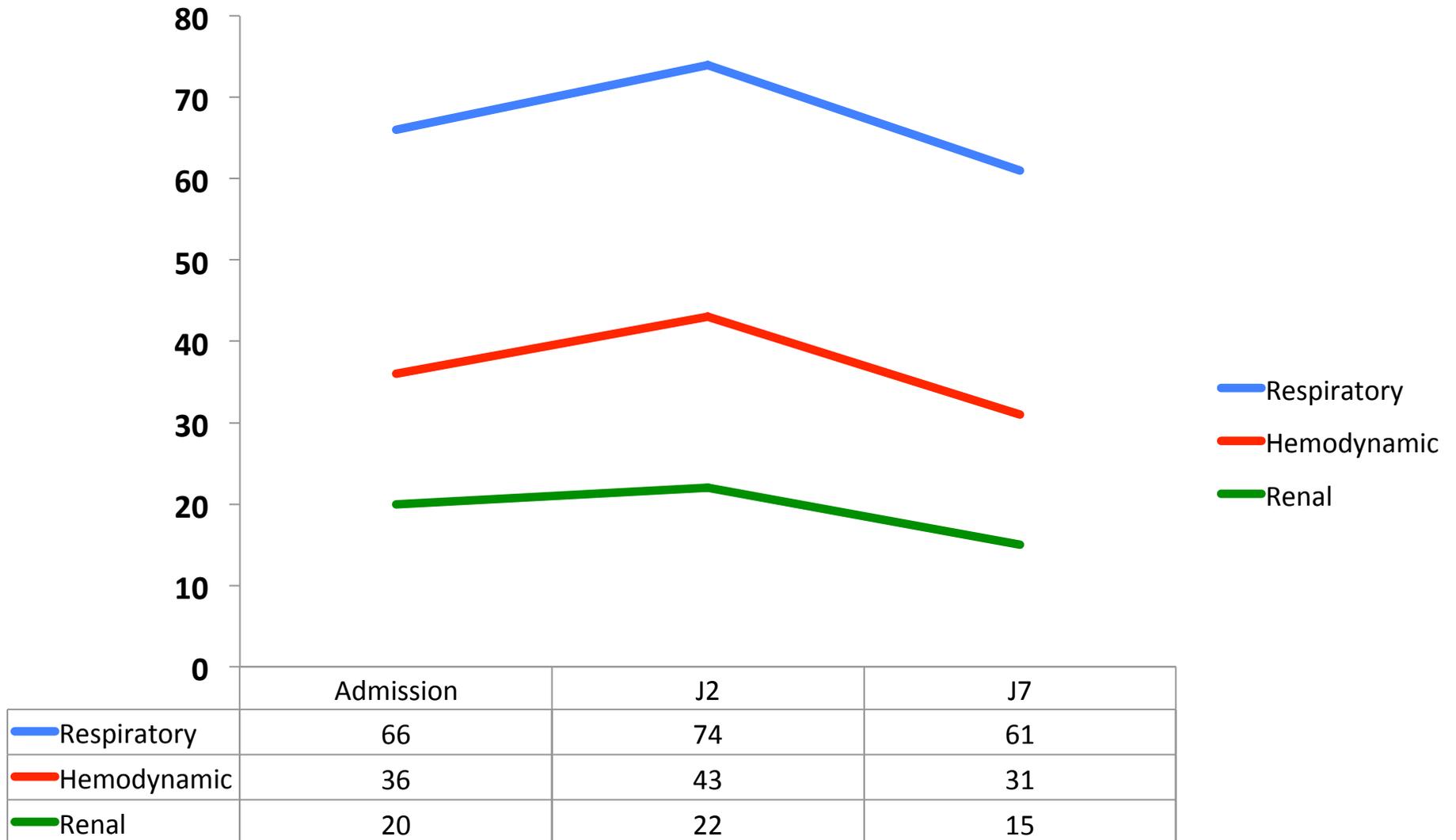
2007-2012: 108 patients hospitalisés en réanimation à St Antoine

Chirurgie autre centre = 5  
Perdus de vue = 14  
PA post-opératoire = 3  
Décès < 48 heures = 3

83 patients  
inclus

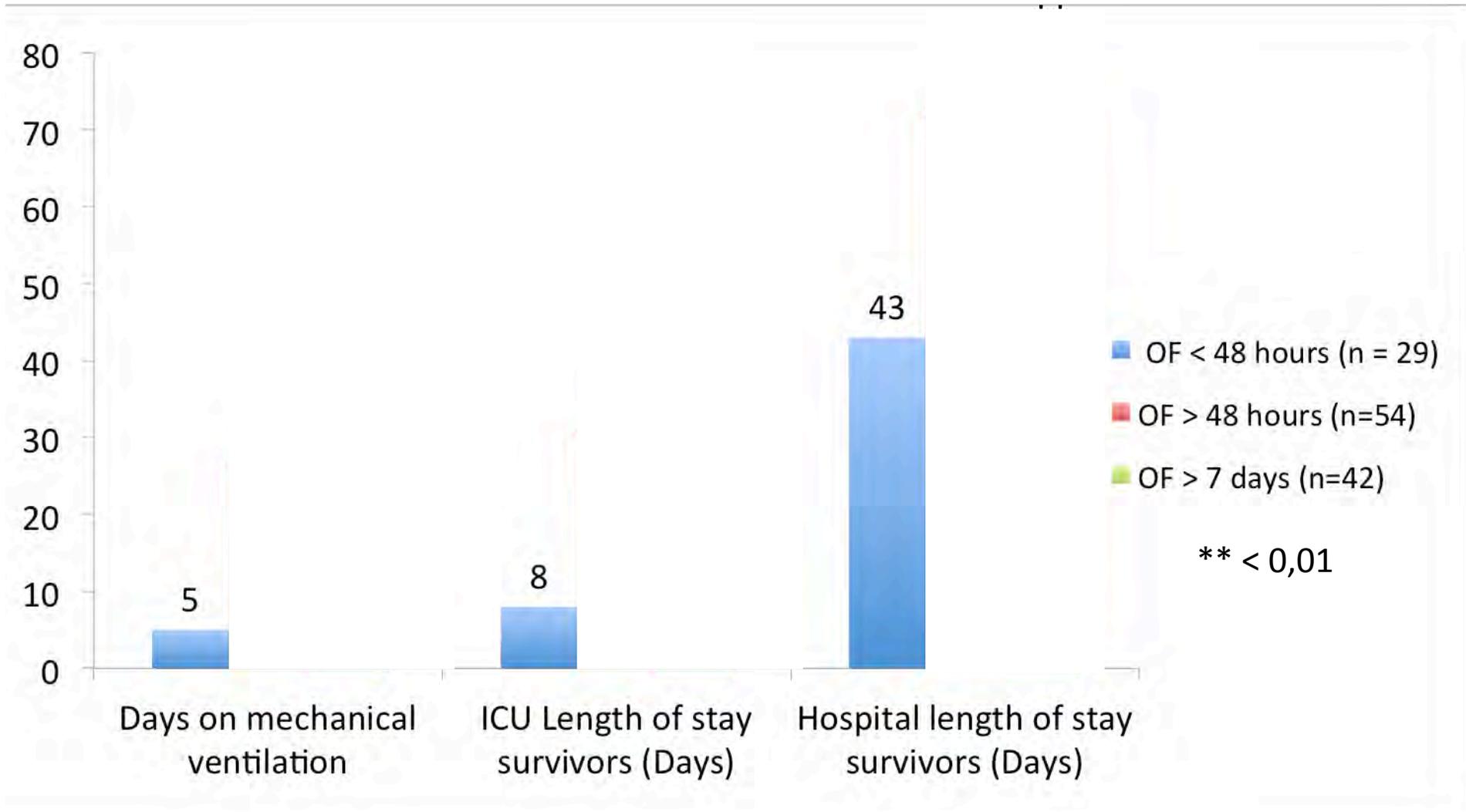
# Apprécier la gravité

Evolution selon le type de défaillances



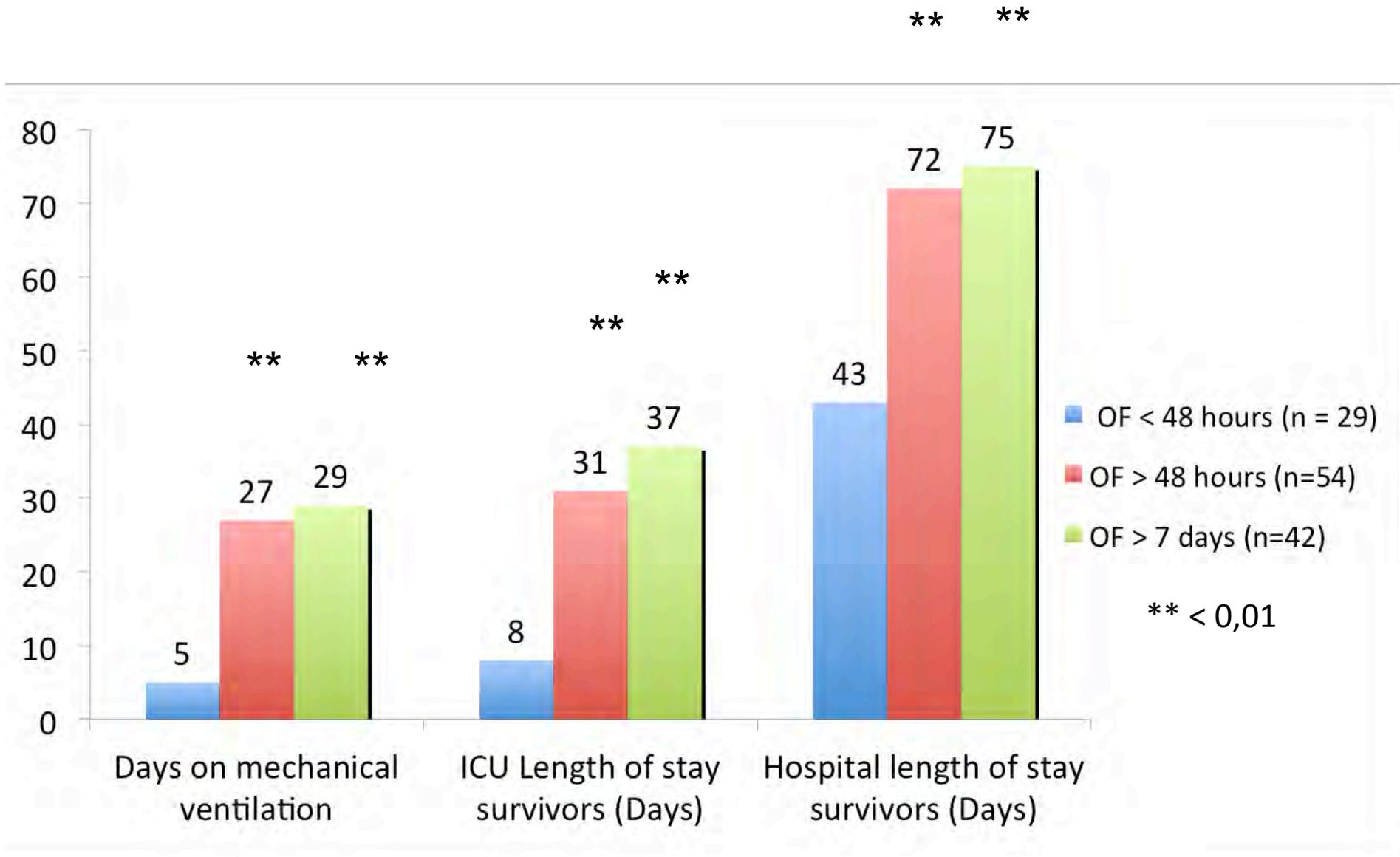
# Apprécier la gravité

Devenir selon la durée de la dysfonction d'organe



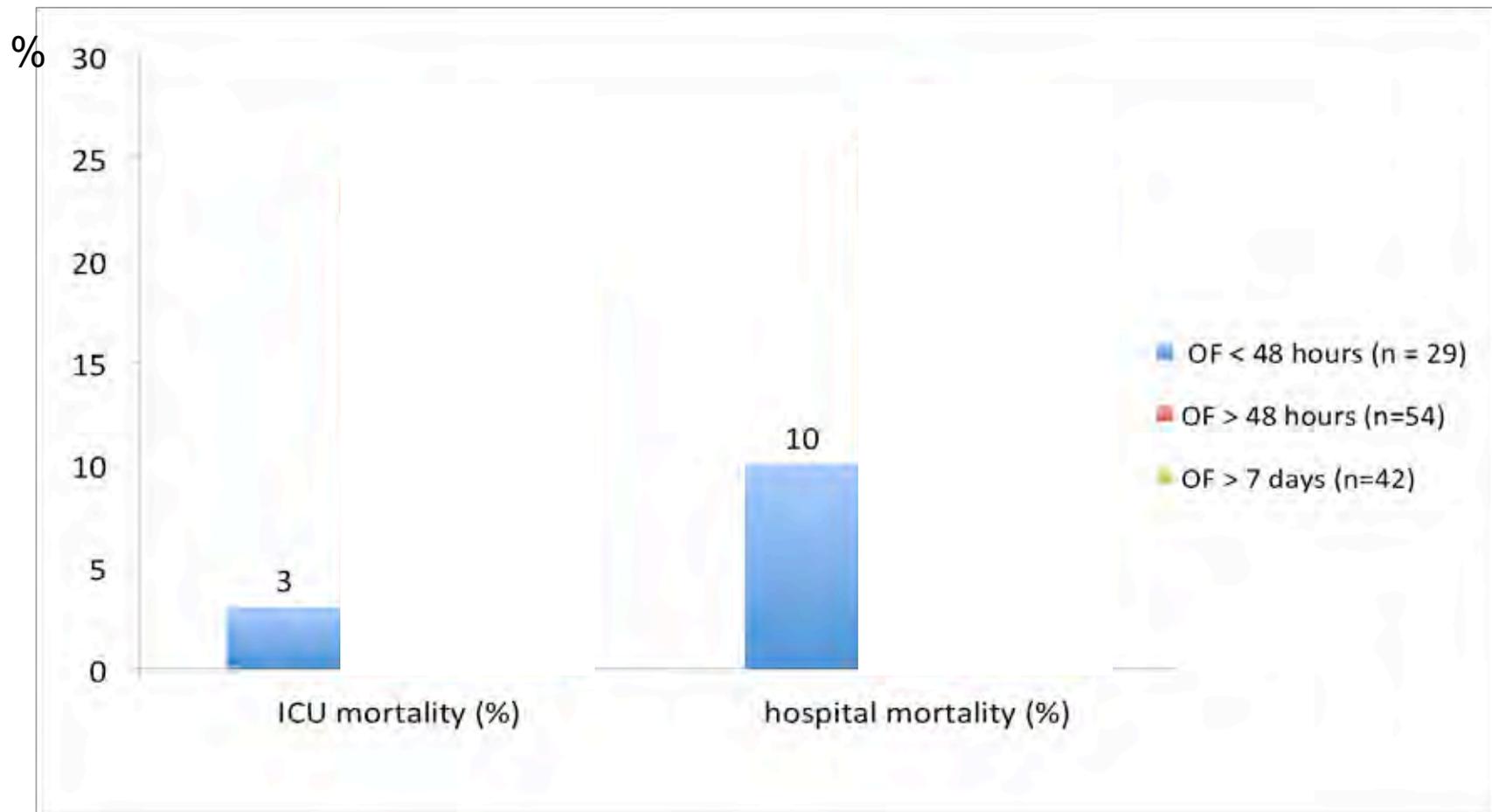
# Apprécier la gravité

Devenir selon la durée de la dysfonction d'organe



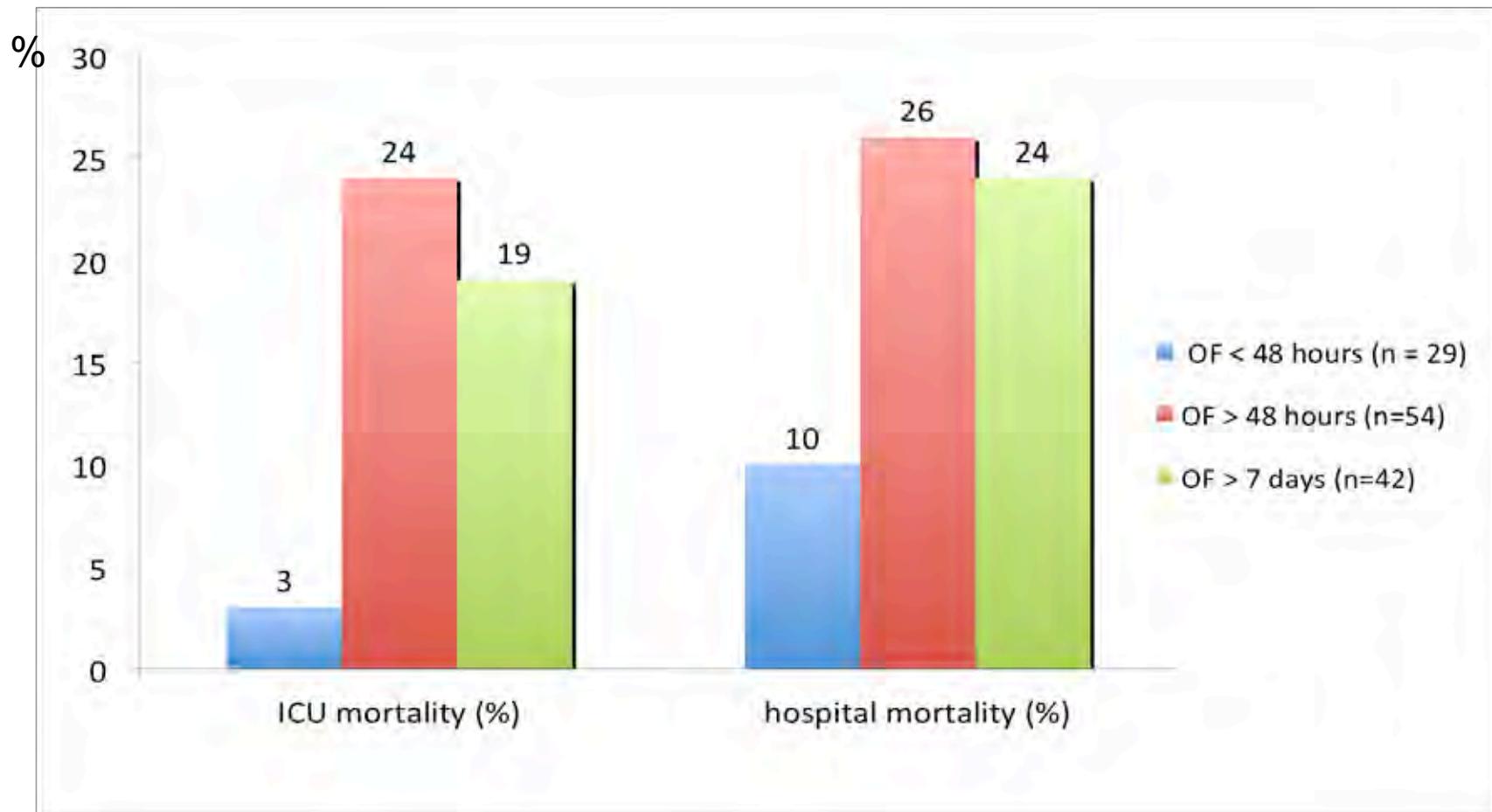
# Apprécier la gravité

Mortalité selon la durée des dysfonction d'organe



# Apprécier la gravité

Mortalité selon la durée des dysfonction d'organe



# Apprécier la gravité

- Apprécier le nombre de défaillances à l'admission
- Admission « large » en « soins aigus »
- Si défaillances non résolues en 48 heures
  - forme sévère à haut risque d'évolution compliquée
  - Transfert en milieu spécialisé

# Prise en charge initiale

- Réanimation
- Analgésie
- Nutrition
- CPRE ?
- Prise en charge des complications: nécrose infectée

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# Défaillance hémodynamique

Vomissements

3<sup>ème</sup> secteur

↓ Resistances  
vasculaires

Atteinte  
myocardique

→ Expansion volémique importante ?

# Défaillance hémodynamique

## American College of Gastroenterology Guideline: Management of Acute Pancreatitis

Scott Tenner, MD, MPH, FACC<sup>1</sup>, John Baillie, MB, ChB, FRCP, FRCG<sup>2</sup>, John DeWitt, MD, FACP<sup>3</sup> and Santhi Swaroop Vege, MD, FACP<sup>4</sup>

### Initial management

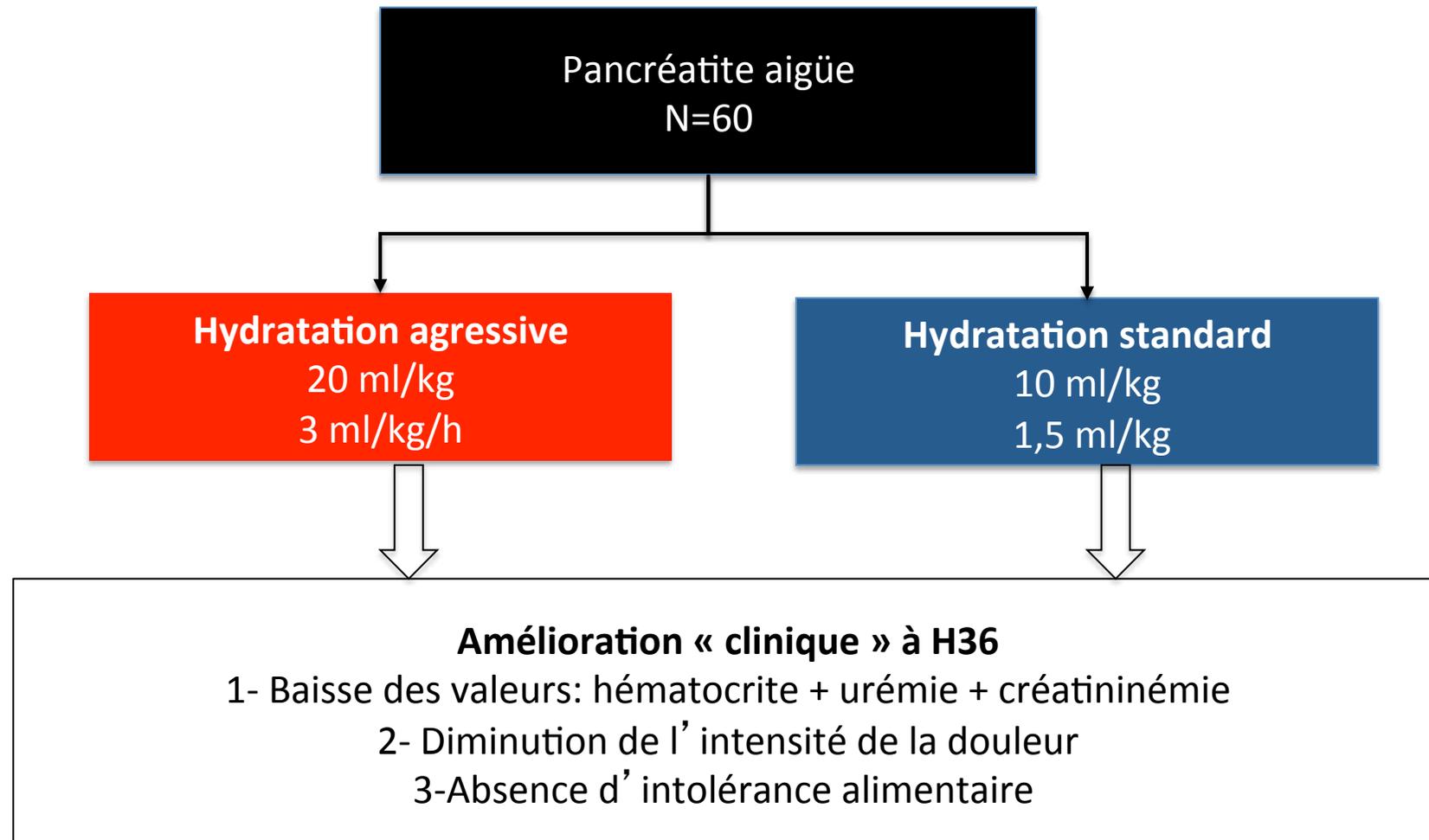
12. Aggressive hydration, defined as 250-500 ml per hour of isotonic crystalloid solution should be provided to all patients, unless cardiovascular and/or renal comorbidities exist. Early aggressive intravenous hydration is most beneficial the first 12-24 h, and may have little benefit beyond (strong recommendation, moderate quality of evidence).

Auteur	Journal	Méthode	Patients	Resultats
Gardner et col.	Pancreatology 2009	Retrospective	35	Mortalité diminuée si 1/3 des apports liquidiens des 72 premières heures reçu en 24h
Wandorf et col.,	Clin Gastro Hep 2011	Retrospective	340	DMS, OF diminuées si 1/3 des apports liquidiens des 72 premières heures reçus en 24 h
Wall et col.,	Pancreas 2011	Avt-Après 1998 - 2008	173	Réduction de la mortalité attribuée à une stratégie d'expansion volémique moins agressive (188 Vs 221 ml/h)
De Madaria	Am J Gastro 2011	Observ	247	Expansion volémique > 4 litres => OF plus fréquentes
Eckerwall	Clinical Nutrition 2006	Retrospective	99	Expansion volémique > 4 litres => Complications respiratoires => ICU plus fréquente

# Early Aggressive Hydration Hastens Clinical Improvement in Mild Acute Pancreatitis

James L. Buxbaum, MD<sup>1</sup>, Michael Quezada, MD<sup>1</sup>, Ben Da, MD<sup>1</sup>, Niraj Jani, MD<sup>1</sup>, Christianne Lane, PhD<sup>2</sup>, Didi Mwendela, MD<sup>1</sup>, Thomas Kelly, MD<sup>1</sup>, Paul Jhun, MD<sup>3</sup>, Kiran Dhanireddy, MD<sup>4</sup> and Loren Laine, MD<sup>5,6</sup>

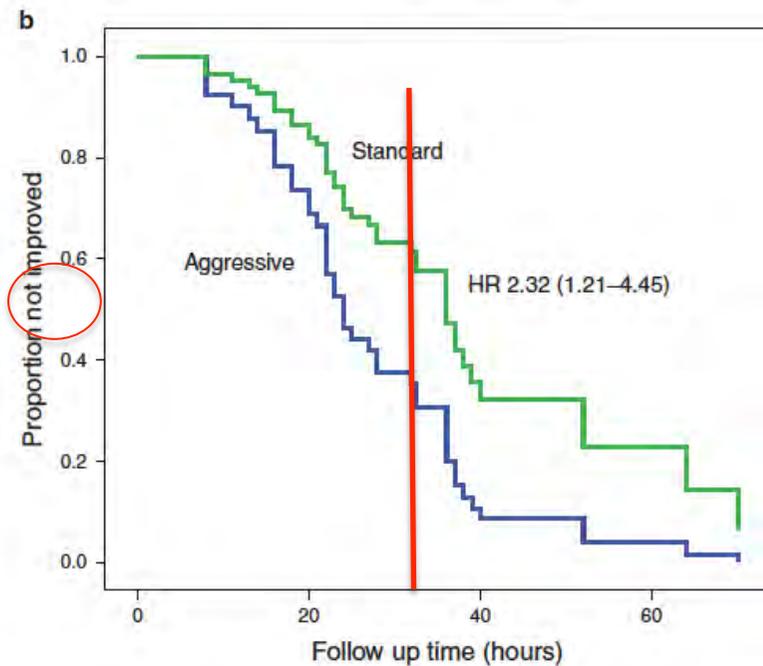
The American Journal of GASTROENTEROLOGY MAY 2017



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The American Journal of GASTROENTEROLOGY MAY 2017



**Table 2.** Secondary outcomes in randomized groups: crude proportions and adjusted odds ratio (logistic regression analysis with covariate of elevated white blood cell count)

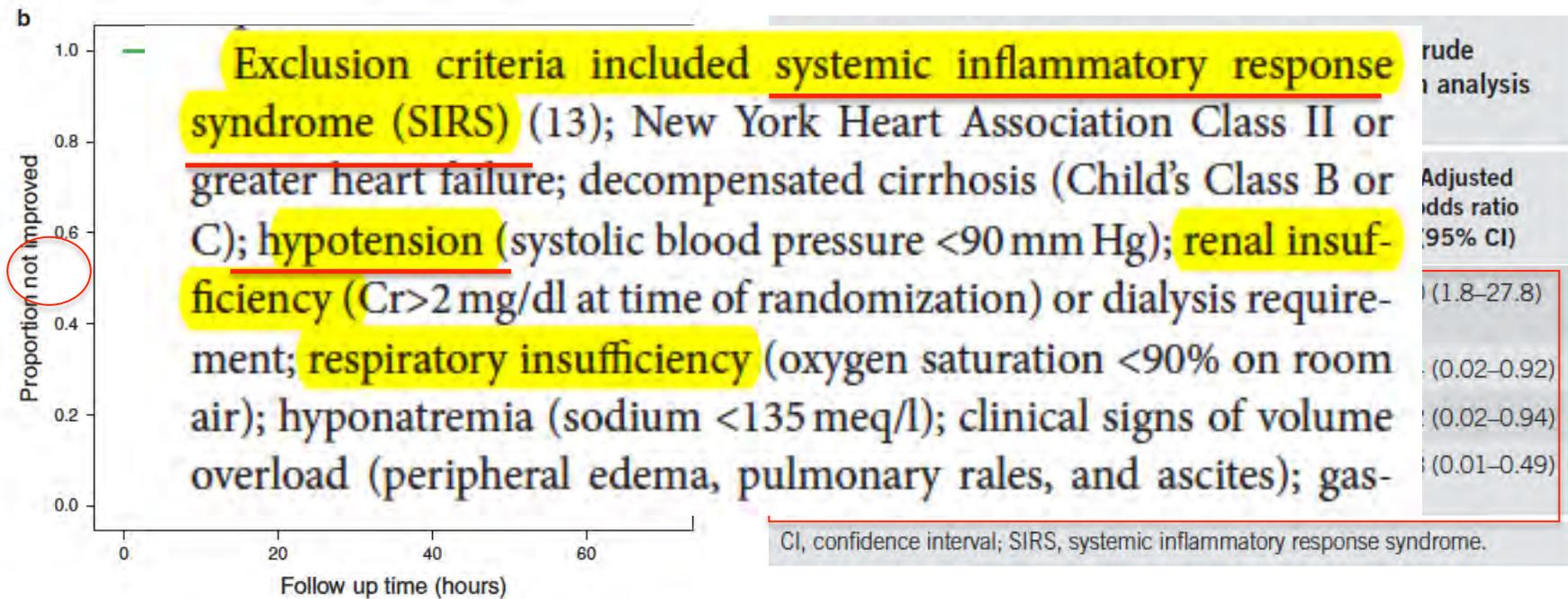
	Aggressive hydration (N=27)	Standard hydration (N=33)	Adjusted odds ratio (95% CI)
Clinical Improvement within 36 h	19 (70%)	14 (42%)	7.0 (1.8–27.8)
Development of SIRS	4 (14.8%)	9 (27.3%)	0.14 (0.02–0.92)
Persistent SIRS	2 (7.4%)	7 (21.2%)	0.12 (0.02–0.94)
Development of hemoconcentration	3 (11.1%)	12 (36.4%)	0.08 (0.01–0.49)

CI, confidence interval; SIRS, systemic inflammatory response syndrome.

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The American Journal of GASTROENTEROLOGY MAY 2017



# Prise en charge initiale

- Réanimation
- **Analgésie**
- Nutrition
- CPRE ?
- Prise en charge des complications: nécrose infectée

# Analgésie péridurale

Effets anti-inflammatoires ?

Amélioration des débits sanguins splanchniques et pancréatiques ?

D24 CRITICAL CARE: THE OTHER HALF OF THE ICU - UPDATE IN MANAGEMENT OF NON-PULMONARY CRITICAL CARE / Poster Discussion Session / Wednesday, May 24/15  
AM: 11:15 AM / Room 151 A (Middle Building, Street Level) Walter E. Washington Convention Center

### Thoracic Epidural Analgesia And Survival In Acute Pancreatitis: A Multicenter Propensity Analysis

M. Jabaudon<sup>1</sup>, N. Belhadj-Tahar<sup>2</sup>, T. Rimmelé<sup>3</sup>, O. Joannes-Boyau<sup>4</sup>, S. Bulyez<sup>5</sup>, C. Roger<sup>6</sup>, Y. Malledant<sup>7</sup>, M. Leone<sup>8</sup>, P. Abback<sup>9</sup>, F. Tamion<sup>10</sup>, H. Dupont<sup>11</sup>, B. Lortat-Jacob<sup>12</sup>, P. Guerci<sup>13</sup>, T. Kerfene<sup>14</sup>, R. Cinotti<sup>15</sup>, L. Jacob<sup>16</sup>, P. Verdier<sup>17</sup>, T. Dugernier<sup>18</sup>, B.

**1003 patients** (64.2% men, mean age 57.6 years) were admitted to the ICU with the diagnosis of AP and enrolled in the study. 190 patients (19%) died within 30 days from admission, 46 patients (from 6 ICUs) received thoracic EA during the management of AP. EA was associated with reduced mortality in unadjusted analyses (4% vs 20%,  $P=0.003$ ). After adjustment for baseline variables associated with mortality (including older age, preexisting chronic cardiovascular or respiratory diseases, sepsis, pneumonia, need for oxygen therapy, invasive or noninvasive mechanical ventilation, acute respiratory distress syndrome, acute kidney injury, need for vasopressor support at baseline), EA was still an independent predictor of 30-day mortality (adjusted Odds Ratio (OR) 0.10; [95% CI 0.02-0.49];  $P=0.004$ ). Using propensity score analysis, the risk of all-cause 30-day mortality in patients with AP receiving EA was significantly lower than that in matched patients who did not receive EA (2% vs 19%,  $P=0.01$ ).

Acute pancreatitis (AP) is a major gastrointestinal disease that is associated with high mortality rates in its most severe forms. Recent preclinical and clinical data suggest that epidural analgesia (EA), a technique primarily aimed at decreasing pain, might improve clinical outcome through anti-inflammatory effects or enhanced splanchnic and pancreatic blood flow.

#### METHODS

We conducted a retrospective, observational cohort study from June 2009 to March 2014 at 17 French and Belgian intensive care units (ICU) to study the impact of EA on survival in adult patients admitted to the ICU with AP. Data were recorded from medical files for each patient. Propensity analyses were used to control for bias in treatment assignment and prognostic imbalances. Main outcome was all-cause mortality at 30 days after ICU admission.

#### RESULTS

**1003 patients** (64.2% men, mean age 57.6 years) were admitted to the ICU with the diagnosis of AP and enrolled in the study. 190 patients (19%) died within 30 days from admission. 46 patients (from 6 ICUs) received thoracic EA during the management of AP. EA was associated with reduced mortality in unadjusted analyses (4% vs 20%,  $P=0.003$ ). After adjustment for baseline variables associated with mortality (including older age, preexisting chronic cardiovascular or respiratory diseases, sepsis, pneumonia, need for oxygen therapy, invasive or noninvasive mechanical ventilation, acute respiratory distress syndrome, acute kidney injury, need for vasopressor support at baseline), EA was still an independent predictor of 30-day mortality (adjusted Odds Ratio (OR) 0.10; [95% CI 0.02-0.49];  $P=0.004$ ). Using propensity score analysis, the risk of all-cause 30-day mortality in patients with AP receiving EA was significantly lower than that in matched patients who did not receive EA (2% vs 19%,  $P=0.01$ ).

#### CONCLUSION

Among critically ill patients with AP, survival at 30 days was better in patients who received EA than in comparable patients who did not. These findings support ongoing research on the use of EA as a therapeutic intervention in AP.

Open Access Protocol

## BMJ Open Epidural analgesia in critically ill patients with acute pancreatitis: the multicentre randomised controlled EPIPAN study protocol

Stéphane Bulyez,<sup>1</sup> Bruno Pereira,<sup>2</sup> Elodie Caumont,<sup>2</sup> Etienne Imhoff,<sup>1</sup> Laurence Roszyk,<sup>3,4</sup> Lise Bernard,<sup>1,5</sup> Leo Bühler,<sup>7</sup> Claudia Heidegger,<sup>6</sup> Samir Jaber,<sup>8</sup> Jean-Yves Lafrant,<sup>10</sup> Russell Chabanne,<sup>1</sup> Pierre-Marie Bertrand,<sup>9</sup> Pierre-François Latens,<sup>12</sup> Philippe Guerci,<sup>13</sup> Pierre-Eric Darin,<sup>14</sup> Etienne Escudier,<sup>11</sup> Achille Sossou,<sup>16</sup> Dominique Morand,<sup>2</sup> Vincent Sapin,<sup>14</sup> Jean-Michel Constantin,<sup>14</sup> Matthieu Jabaudon,<sup>14</sup> on behalf of the EPIPAN study group and the AduRea network

**Background:** Acute pancreatitis (AP) is associated with high morbidity and mortality in its most severe forms. Most patients with severe AP require intubation and invasive mechanical ventilation, frequently for more than 7 days, which is associated with the worst outcome. Recent increasing evidence from preclinical and clinical studies support the beneficial effects of epidural analgesia (EA) in AP, such as increased gut barrier function and splanchnic perfusion, decreased liver damage and inflammatory response, and reduced mortality. Because recent studies suggest that EA might be a safe procedure in the critically ill, we sought to determine whether EA reduced AP-associated respiratory failure and other major clinical outcomes in patients with AP.

**Methods and analysis:** The Epidural Analgesia for Pancreatitis (EPIPAN) trial is an investigator-initiated, prospective, multicentre, randomised controlled two-arm trial with assessor-blinded outcome assessment. The EPIPAN trial will randomise 148 patients with AP requiring admission to an intensive care unit (ICU) to receive EA (with patient-controlled epidural administration of ropivacaine and sufentanil) combined with standard care based on current recommendations on the treatment of AP (interventional group), or standard care alone (reference group). The primary outcome is the number of ventilator-free days at day 30. Secondary outcomes include main complications of AP (eg, organ failure and mortality among others), levels of biological markers of systemic inflammation, epithelial lung injury, renal failure, and healthcare-associated costs.

**Ethics and dissemination:** The study was approved by the appropriate ethics committee (GPP Soc-Ed-18, informed consent is required. If the combined application of EA and standard care proves superior to standard care alone in patients with AP in the ICU, the use of EA may become standard practice in experienced centres, thereby decreasing potential complications related to AP and its burden in critically ill patients. The results will be disseminated in a peer-reviewed journal.

**Strengths and limitations of this study**

- This is the first randomised controlled trial to investigate the effects of epidural analgesia (EA) on organ failure, mortality and clinical outcomes in critically ill patients with acute pancreatitis (AP) (enrolled in a total of 11 French, Belgian and Swiss intensive care units).
- Other strengths are the hypotheses performed around gut leak, respiratory rigidity and assessment, as routine clinical practice.
- In addition, our study includes the collection of a bank of plasma and urine sampled over the last week after inclusion, in order to assess the effects of EA on biological markers of inflammation, lung injury and renal failure.
- One limitation of the study is that the physicians are aware of the group of inclusion. However, outcomes of study outcomes and biological measures are independent observations who do not know the group of inclusion.
- Another limitation may include some generalisability of results from this study to hypotensive patients, because EA is a technique that is restricted to experienced anaesthetists and intensivists.
- Finally, some could highlight the potential risks associated with EA in critically ill patients with hypovolaemic conditions, such as AP, although previous studies have reported good feasibility and safety of EA in this setting. This trial will provide additional data on the safety of EA in ICU patients.

**Trial registration number:** NCT02126332

**INTRODUCTION**  
**Background and rationale**  
Acute pancreatitis (AP) is one of the most frequent gastrointestinal diseases, whose

# Prise en charge initiale

- Réanimation
- Analgésie
- **Nutrition**
- CPRE ?
- Prise en charge des complications: nécrose infectée

# Guidelines for the Provision and Assessment of Nutrition Support Therapy in the Adult Critically Ill Patient:

Journal of Parenteral and Enteral Nutrition  
Volume 33 Number 3  
May/June 2009 277-316  
© 2009 American Society for Parenteral and Enteral Nutrition and Society of Critical Care Medicine  
10.1177/0148607109335234  
<http://jpen.sagepub.com>  
hosted at  
<http://online.sagepub.com>

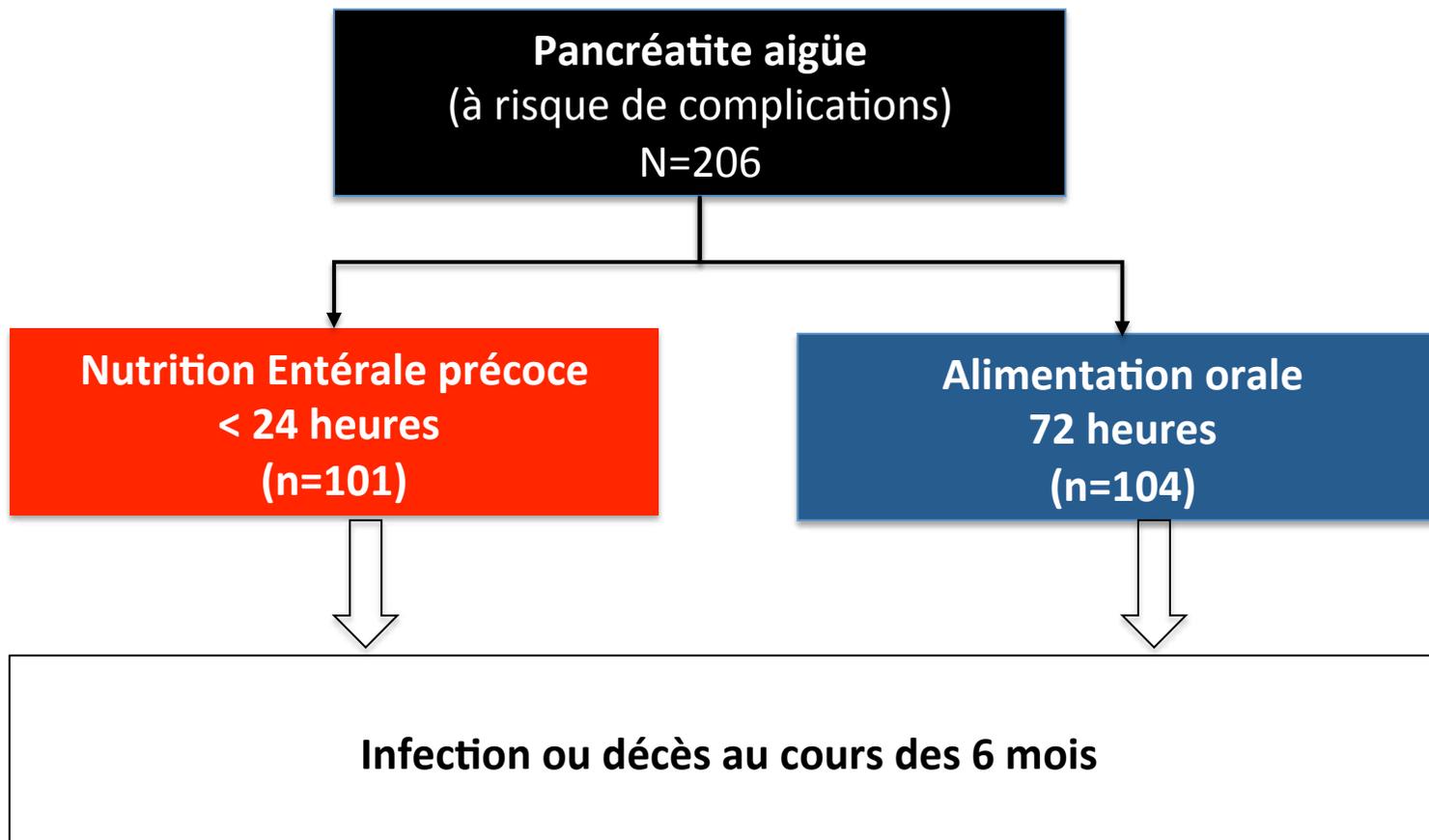
Society of Critical Care Medicine (SCCM) and American Society for Parenteral and Enteral Nutrition (A.S.P.E.N.)

- *Patients with severe acute pancreatitis should have a **nasoenteric tube placed** and **EN** initiated as soon as fluid volume resuscitation is complete. (Grade: C)*
- *Patients with **mild to moderate acute pancreatitis do not require nutrition support therapy** (unless an unexpected complication develops or there is failure to advance to oral diet within 7 days). (Grade: C)*
- *Patients with severe acute pancreatitis may be fed enterally by the **gastric or jejunal route**. (Grade: C)*

# Early versus On-Demand Nasoenteric Tube Feeding in Acute Pancreatitis

O.J. Bakker, S. van Brunschot, H.C. van Santvoort, M.G. Besselink, T.L. Bollen, M.A. Boermeester, C.H. Dejong, H. van Goor, K. Bosscha, U. Ahmed Ali, S. Bouwense, W.M. van Grevenstein, J. Heisterkamp, A.P. Houdijk, J.M. Jansen, T.M. Karsten, E.R. Manusama, V.B. Nieuwenhuijs, A.F. Schaapherder, G.P. van der Schelling, M.P. Schwartz, B.W.M. Spanier, A. Tan, J. Vecht, B.L. Weusten, B.J. Witteman, L.M. Akkermans, M.J. Bruno, M.G. Dijkgraaf, B. van Ramshorst, and H.G. Gooszen, for the Dutch Pancreatitis Study Group

NEJM 2014

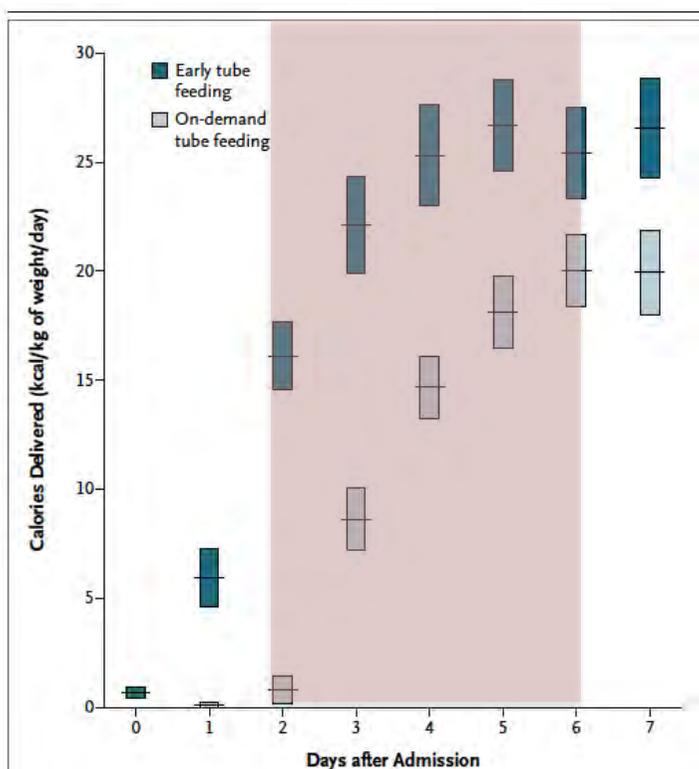


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NEJM 2014



**Table 2. Primary and Secondary End Points, According to the Intention-to-Treat Analysis.\***

Outcome	Early Tube Feeding (N = 101)	On-Demand Tube Feeding (N = 104)	Risk Ratio (95% CI)	P Value
Primary composite end point: infection or death — no. (%)	30 (30)	28 (27)	1.07 (0.79–1.44)	0.76
Secondary end points				
Infection — no. (%)†	25 (25)	27 (26)	0.97 (0.70–1.34)	0.87
Infected pancreatic necrosis	9 (9)	15 (14)	0.74 (0.43–1.26)	0.28
Bacteremia	17 (17)	18 (17)	0.98 (0.68–1.43)	1.00
Pneumonia	12 (12)	13 (12)	0.97 (0.63–1.50)	1.00
Death — no. (%)	11 (11)	7 (7)	1.27 (0.85–1.89)	0.33
Necrotizing pancreatitis — no. (%)‡	64 (63)	65 (62)	1.06 (0.77–1.47)	0.76
CT severity index§	4±2	4±3	—	0.29
ICU admission after randomization — no. (%)	18 (18)	20 (19)	0.95 (0.66–1.38)	0.86
Mechanical ventilation — no. (%)	12 (12)	14 (13)	0.93 (0.60–1.44)	0.84
New-onset organ failure — no./total no. at risk (%)¶				
Single organ failure	26/67 (39)	31/73 (42)	0.92 (0.65–1.32)	0.73
Persistent single organ failure	10/67 (15)	10/73 (14)	1.05 (0.65–1.70)	1.00
Multiple organ failure	7/67 (10)	6/73 (8)	1.14 (0.67–1.95)	0.77
Persistent multiple organ failure	4/67 (6)	4/73 (5)	1.05 (0.51–2.14)	1.00



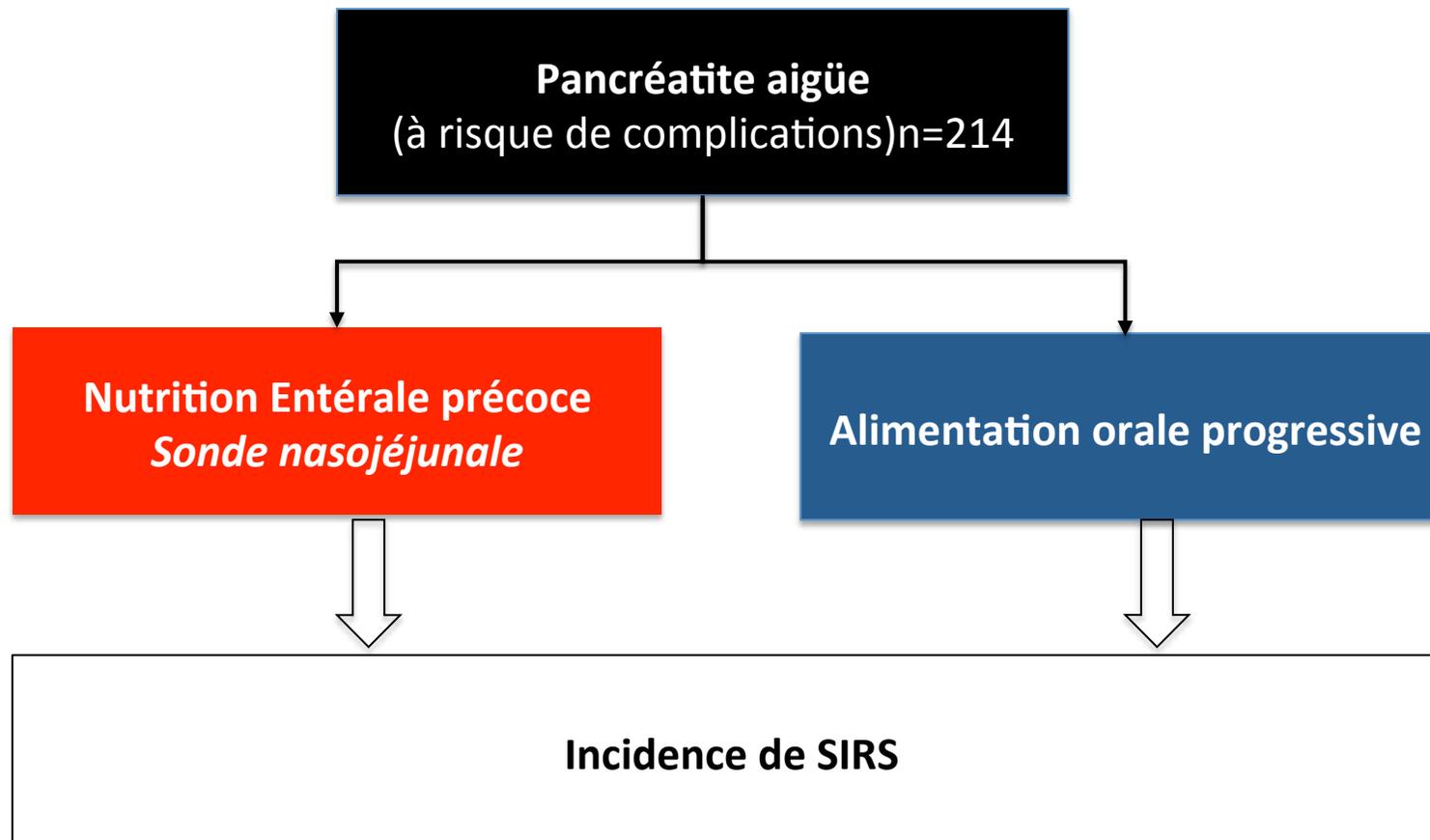
Original article

## Early nasojejunal tube feeding versus nil-by-mouth in acute pancreatitis: A randomized clinical trial

D. Stimac<sup>a</sup>, G. Poropat<sup>a, \*</sup>, G. Hauser<sup>a</sup>, V. Licul<sup>a</sup>, N. Franjic<sup>a</sup>, P. Valkovic Zujic<sup>b</sup>, S. Milic<sup>a</sup>

<sup>a</sup> Department of Gastroenterology, Faculty of Medicine Rijeka, University Hospital Rijeka, Rijeka, Croatia

<sup>b</sup> Department of Radiology, Faculty of Medicine Rijeka, University Hospital Rijeka, Rijeka, Croatia





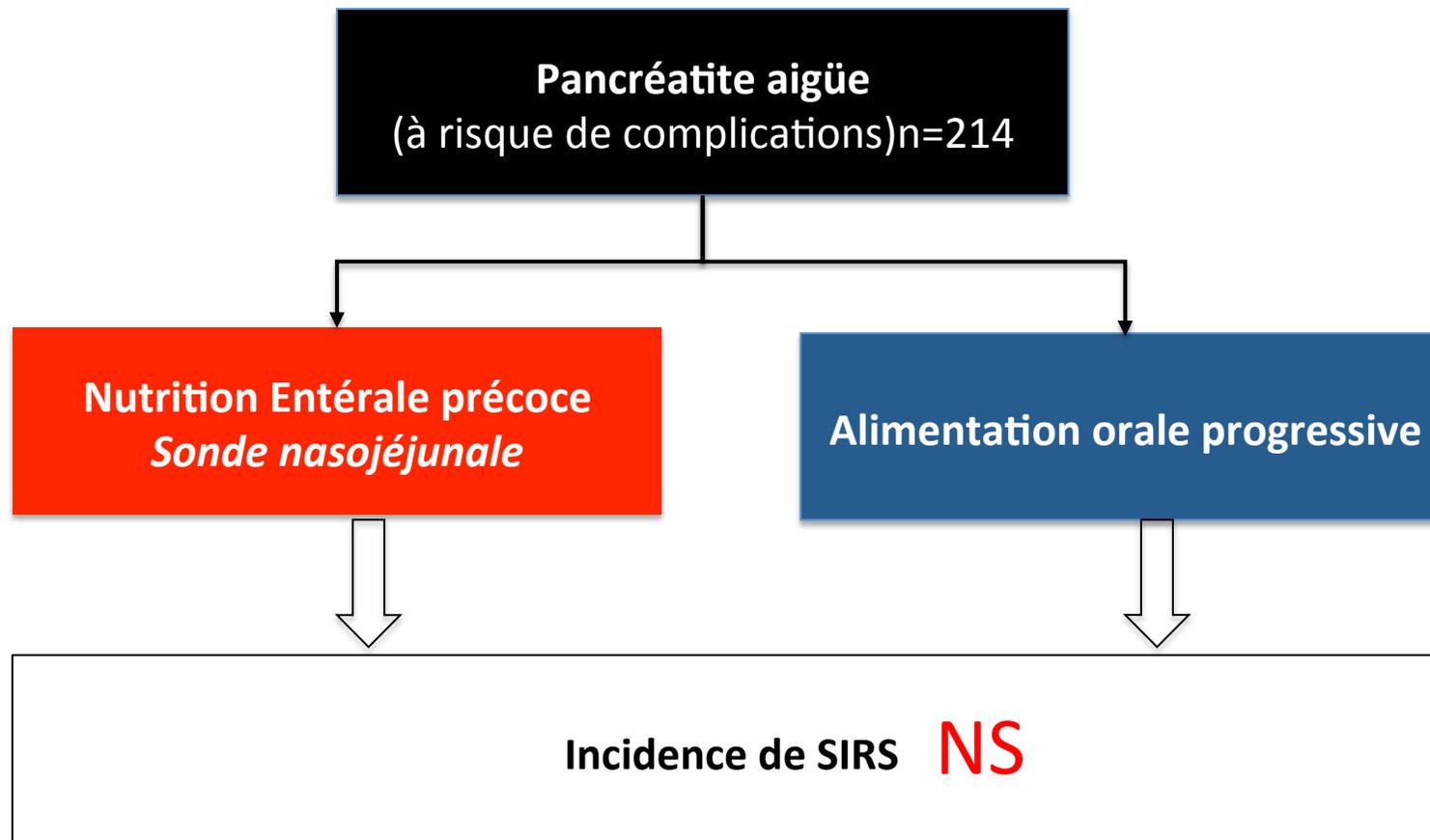
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<sup>a</sup> Department of Gastroenterology, Faculty of Medicine Rijeka, University Hospital Rijeka, Rijeka, Croatia

<sup>b</sup> Department of Radiology, Faculty of Medicine Rijeka, University Hospital Rijeka, Rijeka, Croatia



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

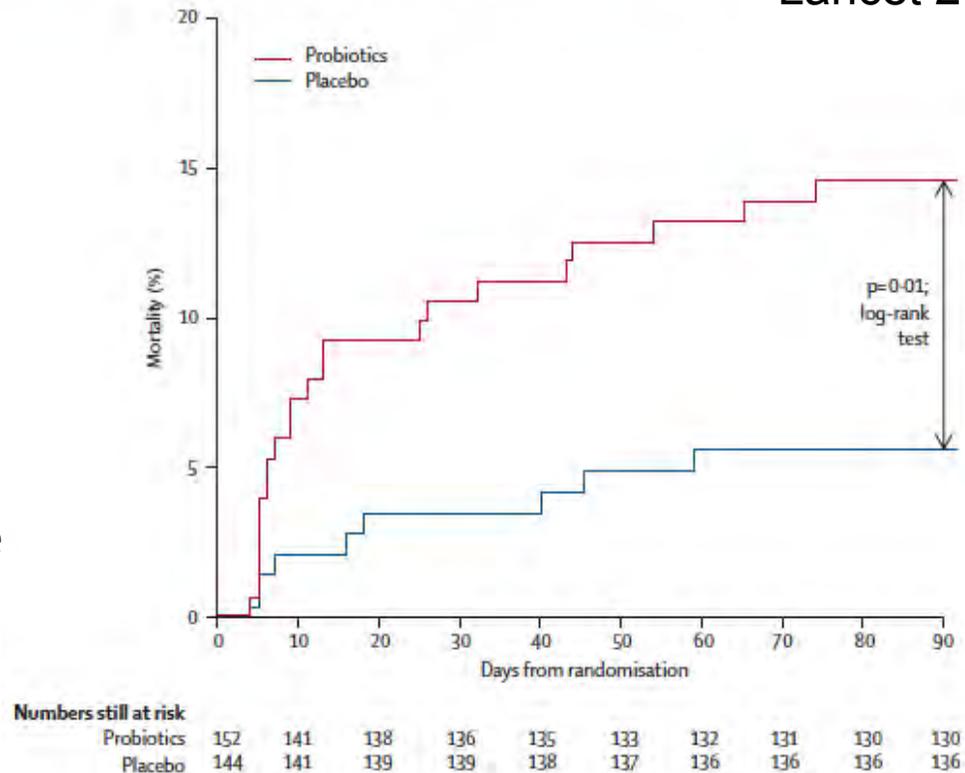
Marc G H Besselink, Hjalmar C van Santvoort, Erik Buskens, Marja A Boermeester, Harry van Goor, Harro M Timmerman, Vincent B Nieuwenhuijs, Thomas L Bollen, Bert van Ramshorst, Ben J M Witterman, Camiel Rosman, Rutger J Ploeg, Menno A Brink, Alexander FM Schaapherder, Cornelis H C Dejong, Peter J Wahab, Cees J H M van Laarhoven, Erwin van der Harst, Casper H J van Eijck, Miguel A Cuesta, Louis M A Akkermans, Hein G Gooszen, for the Dutch Acute Pancreatitis Study Group

Lancet 2008

Probiotique X2/ jours pendant 28j

## Objectifs

- Limiter la prolifération bactérienne
- Limiter la translocation bactérienne
- Améliorer les fonctions immunitaire digestives



**MORTALITE AUGMENTEE**  
**16 vs 9 %, p=0,01**  
**(Ischémie digestive= 9% Vs 0%)**

# Prise en charge initiale

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- Prise en charge des complications: nécrose infectée

# CPRE

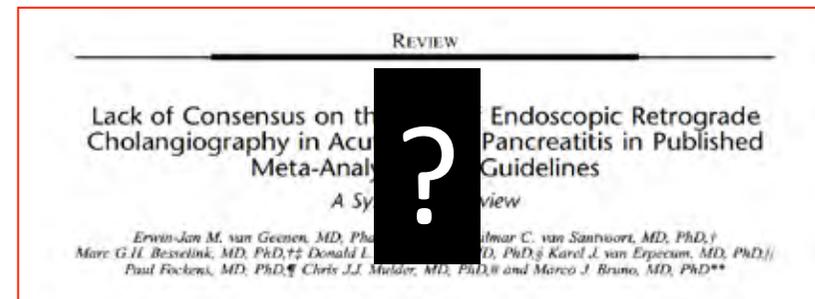
## Pancréatite aiguë biliaire

Angiocholite/obstacle



CPRE + sphinctérotomie

Pas d'angiocholite



*Pancreas* 2013

STUDY PROTOCOL

Open Access



# Early biliary decompression versus conservative treatment in acute biliary pancreatitis (APEC trial): study protocol for a randomized controlled trial



Nicolien J. Schepers<sup>1,2\*</sup>, Olaf J. Bakker<sup>3</sup>, Marc G. H. Besselink<sup>4</sup>, Thomas L. Bollen<sup>5</sup>, Marcel G. W. Dijkgraaf<sup>6</sup>, Casper H. J. van Eijck<sup>7</sup>, Paul Fockens<sup>8</sup>, Erwin J. M. van Geenen<sup>9</sup>, Janneke van Grinsven<sup>4,8</sup>, Nora D. L. Hallensleben<sup>1,10</sup>, Bettina E. Hansen<sup>1</sup>, Hjalmar C. van Santvoort<sup>10</sup>, Robin Timmer<sup>1</sup>, Marie-Paule G. F. Anten<sup>11</sup>, Clemens J. M. Bolwerk<sup>12</sup>, Foke van Delft<sup>13</sup>, Hendrik M. van Dullemen<sup>14</sup>, G. Willemien Erkelens<sup>15</sup>, Jeanin E. van Hooft<sup>8</sup>, Robert Laheij<sup>16</sup>, René W. M. van der Hulst<sup>17</sup>, Jeroen M. Jansen<sup>18</sup>, Frank J. G. M. Kubben<sup>19</sup>, Sjoerd D. Kuiken<sup>20</sup>, Lars E. Perk<sup>21</sup>, Rogier J. J. de Ridder<sup>22</sup>, Mamo C. M. Rijk<sup>23</sup>, Tessa E. H. Römkens<sup>24</sup>, Erik J. Schoon<sup>25</sup>, Matthijs P. Schwartz<sup>26</sup>, B. W. Marcel Spanier<sup>27</sup>, Adriaan C. I. T. L. Tan<sup>28</sup>, Willem J. Thijs<sup>29</sup>, Niels G. Venneman<sup>30</sup>, Frank P. Vleggaar<sup>31</sup>, Wim van de Vrie<sup>32</sup>, Ben J. Witteman<sup>33</sup>, Hein G. Gooszen<sup>34</sup>, Marco J. Bruno<sup>1</sup> and for the Dutch Pancreatitis Study Group

**Methods/Design:** The APEC trial is a randomized controlled, parallel group, superiority multicenter trial. Within 24 hours after presentation to the emergency department, patients with biliary pancreatitis without cholangitis and at high risk for complications, based on an Acute Physiology and Chronic Health Evaluation (APACHE-II) score of 8 or greater, Modified Glasgow score of 3 or greater, or serum C-reactive protein above 150 mg/L, will be randomized. In 27 hospitals of the Dutch Pancreatitis Study Group, 232 patients will be allocated to early ERC with sphincterotomy or to conservative treatment. The primary endpoint is a composite of major complications (that is, organ failure, pancreatic necrosis, pneumonia, bacteremia, cholangitis, pancreatic endocrine, or exocrine insufficiency) or death within 180 days after randomization. Secondary endpoints include ERC-related complications,

# Prise en charge initiale

- Réanimation
- Analgésie
- Nutrition
- CPRE ?
- **Prise en charge des complications: nécrose infectée**

# Infection de nécrose

- Infection de la nécrose pancréatique
- Infections des coulées de nécrose
- Infection du liquide d'ascite
  
- 30 à 50% des PAN
  
- 3<sup>ème</sup> semaine

⇒ **Conditionne le devenir**

⇒ **Modifie la prise en charge**

# Timing and impact of infections in acute pancreatitis

M. G. Besselink<sup>1</sup>, H. C. van Santvoort<sup>1</sup>, M. A. Boermeester<sup>2</sup>, V. B. Nieuwenhuijs<sup>3</sup>, H. van Goor<sup>4</sup>, C. H. C. Dejong<sup>6</sup>, A. F. Schaapherder<sup>5</sup> and H. G. Gooszen<sup>1</sup> for the Dutch Acute Pancreatitis Study Group

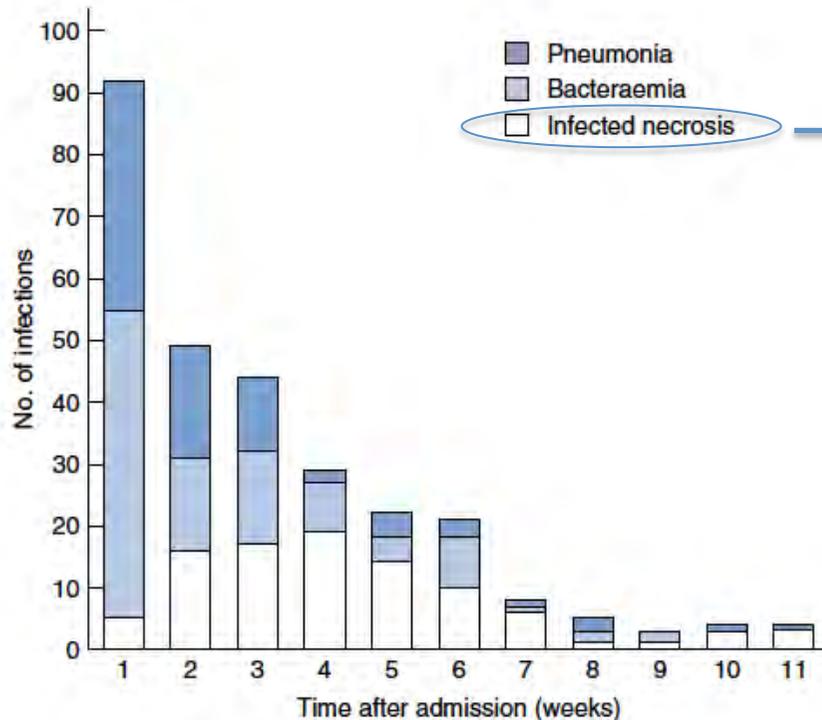
*British Journal of Surgery* 2009; 96: 267–273

731 Patients

154 PAN

72 infections de nécrose pancréatique

- 26 (IQR 17-37) jours après l' admission
- ↑ avec le % de nécrose



Mortalité = 30% (vs 5,1%)

# Antibioprophylaxie ?

Commentary

**A role for prophylactic antibiotics in necrotizing pancreatitis?  
Why we may never know the answer ...**

Jan J De Waele

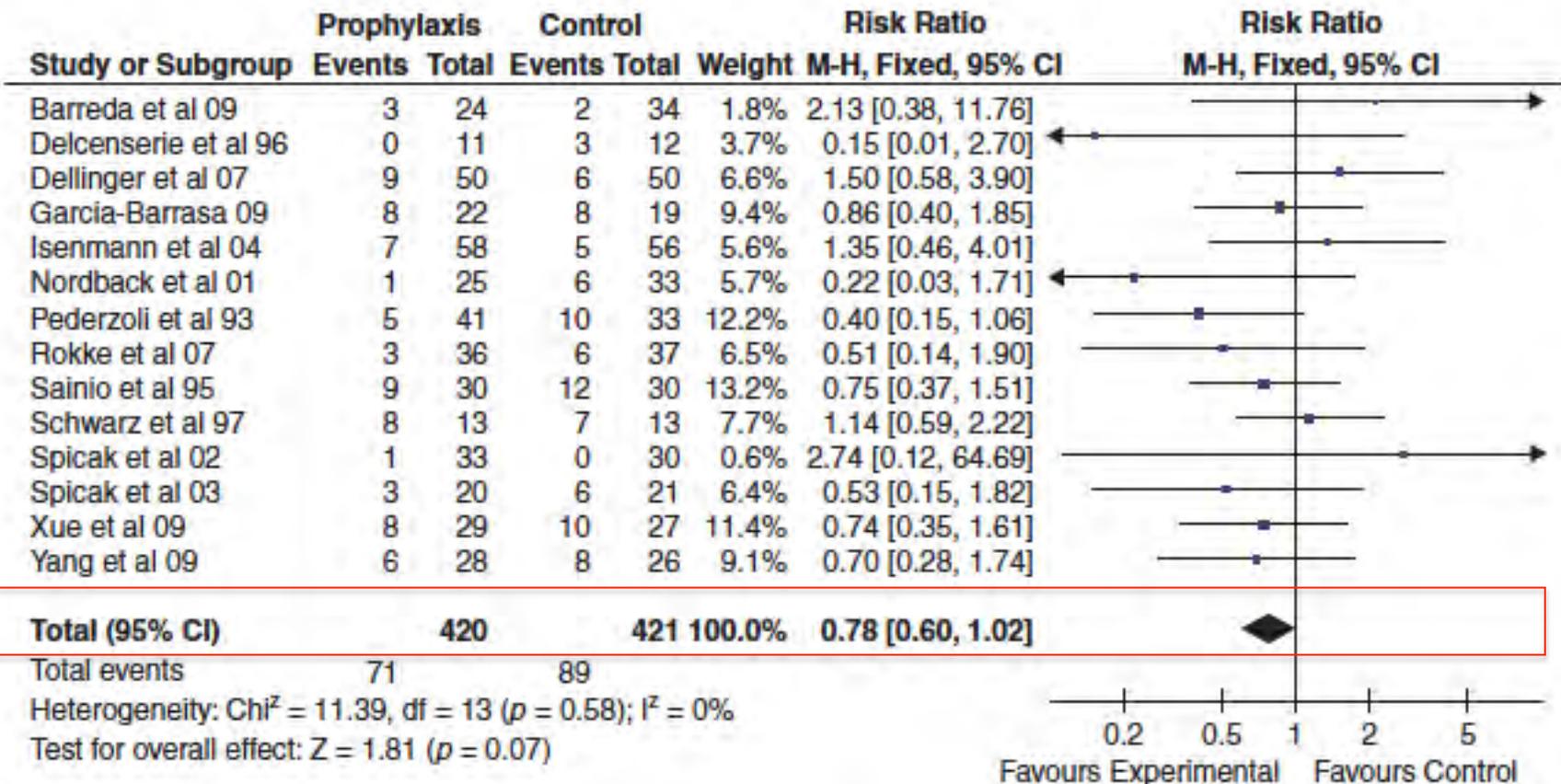
*Critical Care* 2008, **12**:195 (doi:10.1186/cc7122)

# Systematic review and meta-analysis of antibiotic prophylaxis in severe acute pancreatitis

Mathias Wittau, Benjamin Mayer, Jan Scheele, Doris Henne-Bruns, E. Patchen Dellinger & Rainer Isenmann

*Scandinavian Journal of Gastroenterology*, 2011; 46: 261–270

## Infection de nécrose

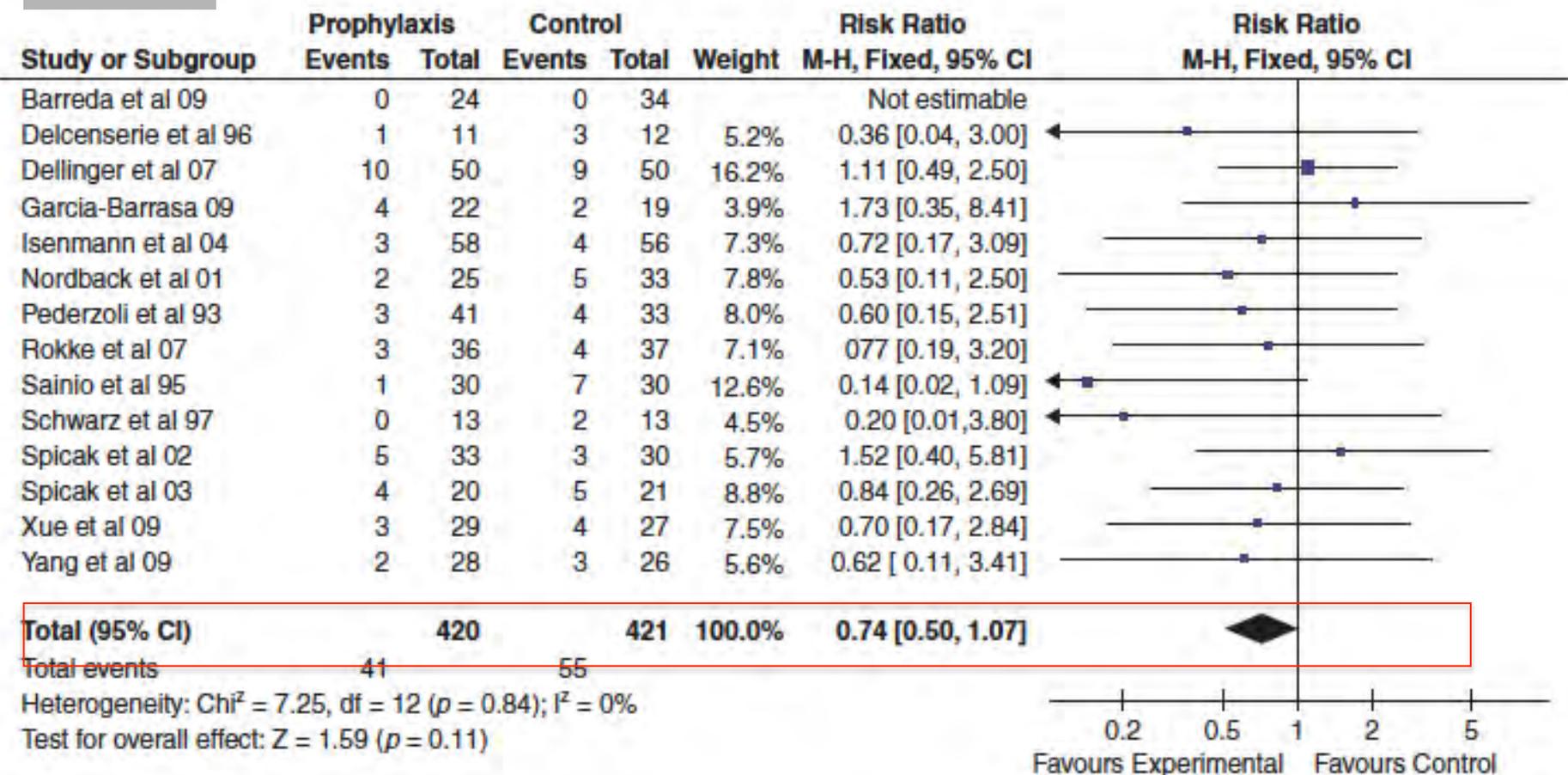


# Systematic review and meta-analysis of antibiotic prophylaxis in severe acute pancreatitis

Mathias Wittau, Benjamin Mayer, Jan Scheele, Doris Henne-Bruns, E. Patchen Dellinger & Rainer Isenmann

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## Mortalité

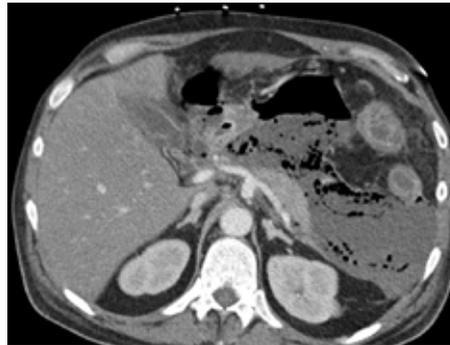


# Diagnostic

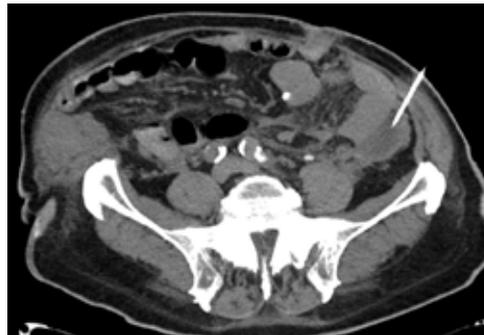
## 1-Suspicion clinique/biologique

- Fièvre
- Hyperleucocytose
- Apparition ou aggravation défaillances viscérales
- Bactériémie à germes digestifs

## 2-Scanographie évocatrice



## 3-Bactérie à l'examen microbiologique d'une ponction de nécrose



# Aspects microbiologiques

- Prélèvements polymicrobiens : 13 à 60 %
- E. coli 30 à 50 %
- Staphylococcus sp 2 à 57 %
- Entérocoques 5 à 40 %
- Pseudomonas sp 0 à 20 %
- Anaérobies 4 à 15 %
- Candida sp 4 à 20 %

# Principes de prise en charge

ISRCTN registry

Search



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ISRCTN33682933 DOI 10.1186/ISRCTN33682933

Postponed or immediate drainage of infected necrotizing pancreatitis (POINTER trial)



CrossMark

**Condition category**

Digestive System

**Date applied**

02/07/2015

**Date assigned**

06/08/2015

**Last edited**

20/03/2017

**Prospective/Retrospective**

Retrospectively registered

**Overall trial status**

Ongoing

**Recruitment status**

Recruiting

# Principes de prise en charge

- **Approche « historique » = Chirurgie**
  - Ventre ouvert (laparostomie) (mortalité 70%)
  - nécrosectomie drainage Simple à ventre fermé (DC 40%)
  - nécrosectomie et irrigation continue des sites de Drainage (DC 10 à 25%)
  - Nécrosectomie retropéritonéale

# Données Historiques

## PANCREATITES AIGUES NECROTIQUES

### DRAINAGE ACTIF PROLONGE ET NUTRITION JEJUNALE CONTINUE (114)

#### Résultats de la chirurgie conventionnelle

##### - Débridement et drainage d'abcès

1981 RANSON	65 % de mortalité
1985 WARSHAW	24 % de mortalité
1988 WILSON and IMRIE	38 % de mortalité

##### - Résection pancréatique

1981 ALEXANDRE	60 % de mortalité
1984 KIVILAAKSO	22% de mortalité
1985 ALDRIDGE	33 % de mortalité
1986 NORDBLACK	43 % de mortalité



Diapositives E. Levy (198X)

# LE DRAINAGE ACTIF PROLONGÉ DES PANCRÉATITES AIGÜES NÉCROTICO-HÉMORRAGIQUES

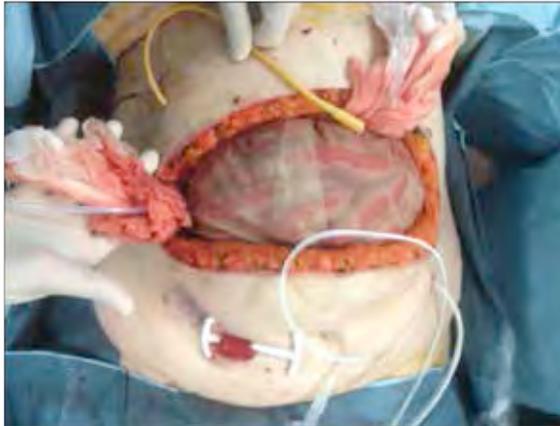
Indications. Techniques. Résultats préliminaires

A propos de vingt-six cas

E. LEVY<sup>1</sup>, L. HANNOUN<sup>2</sup>, R. PARC<sup>3</sup>,  
J. HONIGER<sup>1</sup>, C. HUGUET<sup>2</sup>, J. LOYGUE<sup>2</sup>

ANNALES  
DE CHIRURGIE

VOL. 38. N° 5  
JUIN 1984



# Nécrosectomie rétropéritonéale



# Principes de prise en charge

- **Approche « historique » = Chirurgie**
  - Ventre ouvert (laparostomie) (mortalité 70%)
  - nécrosectomie drainage Simple à ventre fermé (DC 40%)
  - nécrosectomie et irrigation continue des sites de Drainage (DC 10 à 25%)
  - Nécrosectomie rétro-péritonéale
- **Techniques mini-invasives**
  - Drainage scanographique
  - Nécrosectomie rétro-péritonéale sous vidéoscopie
  - Nécrosectomie transgastrique endoscopique

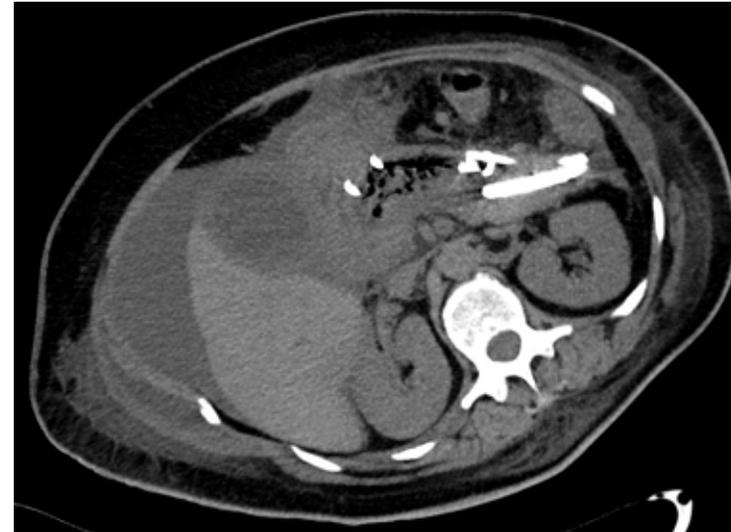
# Drainage percutané

## Systematic review of percutaneous catheter drainage as primary treatment for necrotizing pancreatitis

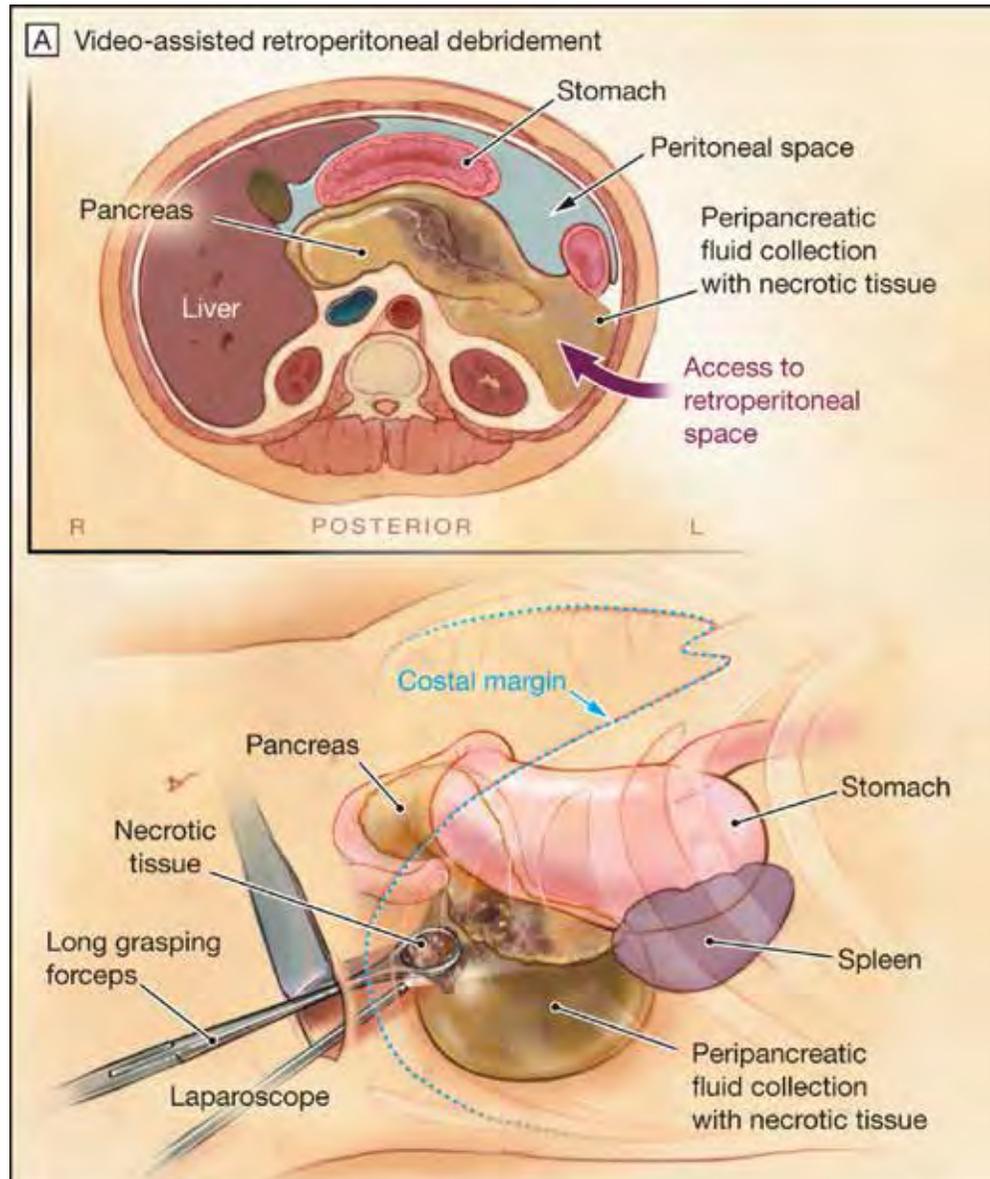
M. C. van Baal<sup>1</sup>, H. C. van Santvoort<sup>1</sup>, T. L. Bollen<sup>2</sup>, O. J. Bakker<sup>1</sup>, M. G. Besselink<sup>1</sup> and H. G. Gooszen<sup>3</sup> for the Dutch Pancreatitis Study Group

*British Journal of Surgery* 2011; **98**: 18–27

- 384 patients/ 11 études
- Drainage de nécrose/collection initialement infectées dans 70% des cas
- 50% de survie sans nécessité de nécrosectomie chirurgicale
- Mortalité = 15 %



# Drainage chirurgicale rétro-péritonéal



## A Step-up Approach or Open Necrosectomy for Necrotizing Pancreatitis

Hjalmar C. van Santvoort, M.D., Marc G. Besselink, M.D., Ph.D.,

NEJM 2010

### APPROCHE MINI-INVASIVE (N=43)

- Drainage percutané
- Drainage rétro-péritonéal sous  
vidéoscopie



Drainage seul dans 35% des cas  
Nécrosectomie retardée dans  
60% des cas

### NÉCROSECTOMIE CHIRURGICALE (N=45)



Ré intervention dans 42% des cas

# A Step-up Approach or Open Necrosectomy for Necrotizing Pancreatitis

Hjalmar C. van Santvoort, M.D., Marc G. Besselink, M.D., Ph.D.,

NEJM 2010

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

# A Step-up Approach or Open Necrosectomy for Necrotizing Pancreatitis

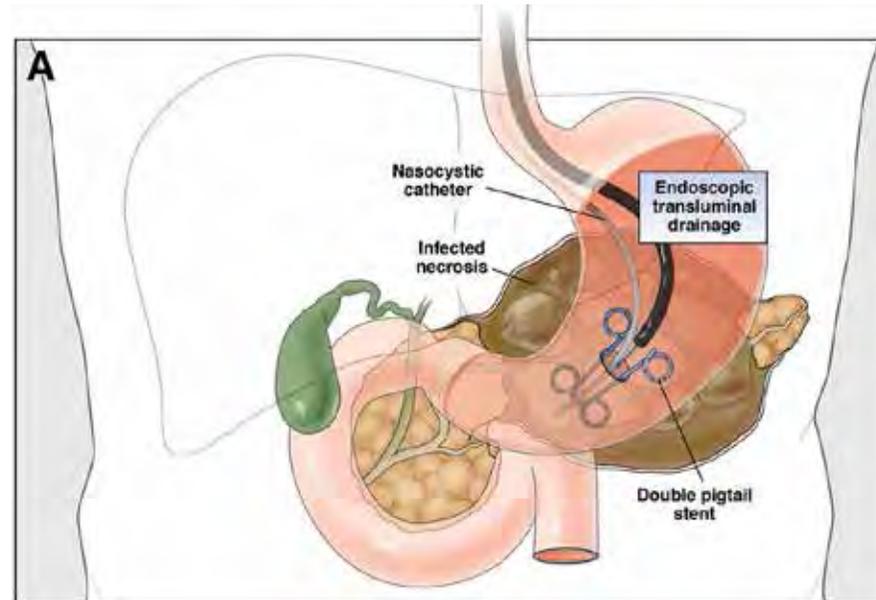
Hjalmar C. van Santvoort, M.D., Marc G. Besselink, M.D., Ph.D.,

NEJM 2010

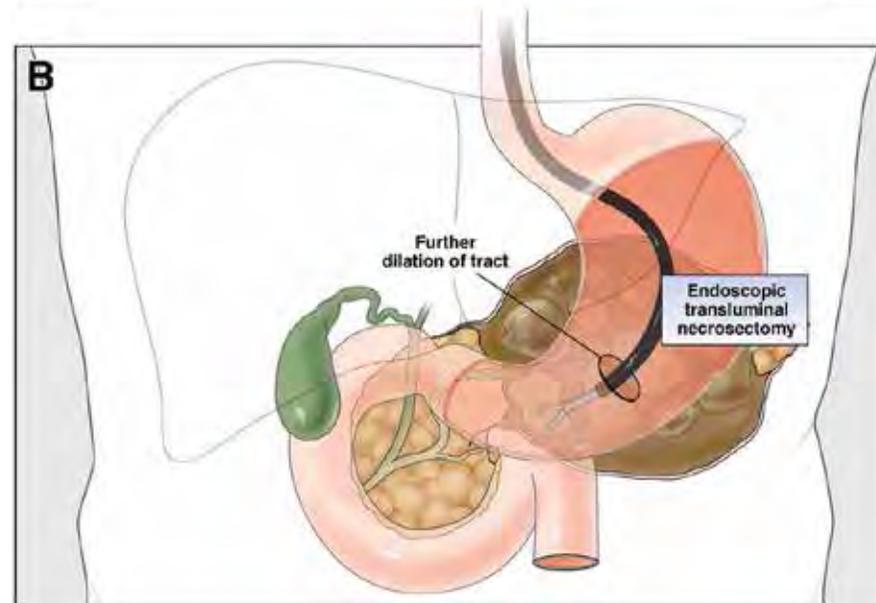
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# Traitement endoscopique

Drainage



Nécrosectomie



# Nécrosectomie endoscopique

## Études multicentriques rétrospectives

	Etude GEPARD*	Etude US**	Etude JENIPaN ***
Patients	93	104	57
Nécrose infectée	76%	42%	100%
Douleurs persistantes	88%	61%	ND
Nombre moyen de séances	6.2 (1-35)	3.7 (1-13)	5 (1-20)
Délai par rapport à la PA	43 jours (11-158)	46 jours (6-510)	50 jours (13-436)
Succès	80%	91.3%	75%
Complications	26%	14%	33%
Mortalité	7.5%	5.7%	11%

Complications : hémorragies mineures ou majeures, perforations péritonéales, fistules, pneumopéritoine, embolies gazeuses.

Seifert H et al. Gut 2009;58:1260-1266; \*\* Gardner TB et al. Gastrointest Endosc 2011;73:718-726

\*\*\* I.Yasuda et al. Endoscopy 2013;45 : 627-634.

# Endoscopic Transgastric vs Surgical Necrosectomy for Infected Necrotizing Pancreatitis

A Randomized Trial

Olaf J. Bakker, MD

JAMA, March 14, 2012—Vol 307, No. 10

## NECROSECTOMIE TRANSGASTRIQUE SOUS ENDOSCOPIE

(n=10)

- Drainage retopéritonéal (n=6)
- Drainage scanographique (n=4)
- 

## NECROSECTOMIE CHIRURGICALE

(n=10)

- Drainage retopéritonéal (n=6)
- Drainage scanographique (n=4)
- 



Critère de jugement

Score composite (**complications** ou **décès**)

IL-6 plasmatique

# Endoscopic Transgastric vs Surgical Necrosectomy for Infected Necrotizing Pancreatitis

A Randomized Trial

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JAMA, March 14, 2012—Vol 307, No. 10

**Table 2.** Clinical End Points<sup>a</sup>

	Surgical Necrosectomy (n = 10)	Endoscopic Transgastric Necrosectomy (n = 10)	Risk Difference (95% CI)	P Value
Major complications or death, No. (%) <sup>b</sup>	8 (80)	2 (20)	0.60 (0.16 to 0.80)	.03
Death, No. (%)	4 (40)	1 (10)	0.30 (−0.08 to 0.60)	.30
Major complications, No. (%)				
New-onset multiple organ failure <sup>c</sup>	5 (50)	0 (0)	0.50 (0.12 to 0.76)	.03
Intra-abdominal bleeding requiring intervention	0 (0)	0 (0)		
Enterocutaneous fistula or perforation of a visceral organ requiring intervention	2 (20)	0 (0)	0.20 (−0.11 to 0.51)	.47
Pancreatic fistula	7 (70)	1 (10)	0.60 (0.17 to 0.81)	.02
Long-term complications, No. (%) <sup>d</sup>	(n = 6)	(n = 9)		
New-onset diabetes	3 (50)	2 (22)	0.28 (−0.17 to 0.63)	.33
Use of pancreatic enzymes	3 (50)	0 (0)	0.50 (0.07 to 0.81)	.04
Persisting fluid collections <sup>e</sup>	3 (50)	2 (22)	0.28 (−0.17 to 0.63)	.33
Health care utilization, No.	(n = 10)	(n = 10)		
No. of necrosectomies, endoscopic or surgical	1 (1 to 2)	3 (2 to 6)		.007
New ICU admission anytime after randomization, No. (%)	5 (50)	1 (10)	0.4 (−0.002 to 0.68)	.14
Days in hospital after randomization <sup>f</sup>	36 (17 to 74)	45 (12 to 69)		.91

➔ Réduction des complications majeures et décès dans le groupe « endoscopie »

# Endoscopic or surgical step-up approach for infected necrotising pancreatitis: a multicentre randomised trial



Lancet nov 2017

*Sandra van Brunschot, Janneke van Grinsven, Hjalmar C van Santvoort, Olaf J Bakker, Marc G Besselink, Marja A Boermeester, Thomas L Bollen, Koop Bosscha, Stefan A Bouwense, Marco J Bruno, Vincent C Cappendijk, Esther C Consten, Cornelis H Dejong, Casper H van Eijck, Willemien G Erkelens, Harry van Goor, Wilhelmina M U van Grevenstein, Jan-Willem Haveman, Sijbrand H Hofker, Jeroen M Jansen, Johan S Laméris, Krijn P van Lienden, Maarten A Meijssen, Chris J Mulder, Vincent B Nieuwenhuijs, Jan-Werner Poley, Rutger Quispel, Rogier J de Ridder, Tessa E Römken, Joris J Scheepers, Nicolien J Schepers, Matthijs P Schwartz, Tom Seerden, BW Marcel Spanier, Jan Willem A Straathof, Marin Strijker, Robin Timmer, Niels G Venneman, Frank P Vleggaar, Rogier P Voermans, Ben J Witteman, Hein G Gooszen, Marcel G Dijkgraaf, Paul Fockens, for the Dutch Pancreatitis Study Group\**

**ENDOSCOPIE  
(n=51)**

**Drainage transgastrique**

**Nécrosectomie transgastrique**

**APPROCHE GRADUEE  
(n=47)**

**Drainage percutané**

**Nécrosectomie chirurgicale  
(abord rétropéritonéal)**

**Complication majeur ou décès**

	Endoscopic step-up approach (n=51)	Surgical step-up approach (n=47)	Relative risk (95% CI)	p value
<b>Primary endpoint</b>				
Major complications or death*	22 (43%)	21 (45%)	0.97 (0.62-1.51)	0.88
<b>Secondary endpoints</b>				
<b>New-onset organ failure†</b>				
Pulmonary	4 (8%)	7 (15%)	0.53 (0.16-1.68)	0.27
Persistent pulmonary	4 (8%)	5 (11%)	0.74 (0.21-2.58)	0.63
Cardiovascular	3 (6%)	9 (19%)	0.31 (0.09-1.07)	0.045
Persistent cardiovascular	2 (4%)	8 (17%)	0.23 (0.05-1.03)	0.032
Renal	2 (4%)	6 (13%)	0.31 (0.07-1.45)	0.11
Persistent renal	2 (4%)	6 (13%)	0.31 (0.07-1.45)	0.11
Single organ failure	7 (14%)	13 (28%)	0.50 (0.22-1.14)	0.087
Persistent single organ failure	6 (12%)	11 (23%)	0.50 (0.20-1.25)	0.13
Multiple organ failure	2 (4%)	6 (13%)	0.31 (0.07-1.45)	0.11
Persistent multiple organ failure	2 (4%)	5 (11%)	0.37 (0.08-1.81)	0.20
Bleeding (requiring intervention)	11 (22%)	10 (21%)	1.01 (0.47-2.17)	0.97
Perforation of a visceral organ or enterocutaneous fistula (requiring intervention)	4 (8%)	8 (17%)	0.46 (0.15-1.43)	0.17
Incisional hernia	0	1 (2%)	..	0.30
Death	9 (18%)	6 (13%)	1.38 (0.53-3.59)	0.50

**Fatal Gas Embolism  
after Endoscopic  
Transgastric  
Necrosectomy for  
Infected Necrotizing  
Pancreatitis**

Benjamin Bonnot, MD<sup>1</sup>,  
Isabelle Nion-Larmurier, MD<sup>2</sup>,  
Benoit Desaint, MD<sup>2</sup>, Najim Chafai, MD<sup>3</sup>,  
François Paye, MD, PhD<sup>3</sup>, Marc Beaussier,  
MD, PhD<sup>1</sup> and Thomas Lescot, MD, PhD<sup>1</sup>

PAN compliquée d'infection de nécrose  
6<sup>ème</sup> séance de nécrosectomie  
ACR per procédure



# Conclusions

- **Pancréatite aigüe sévère:** persistance d'une défaillance d'organe
- **Expansion volémique** sans modification contextuelle
- **Pas d'antibioprophylaxie** en routine
- **Place de l'analgésie péridurale** en cours d'exploration
- **Nutrition artificielle entérale:** sans se presser
- **Stratégies mini invasive** du traitement de l'infection de nécrose
- **Approche multidisciplinaire**
- **Stratification des patients:** à préciser

# Prise en charge des Pancréatites AIGUES nécrosantes

## Algorithme de Saint-Antoine

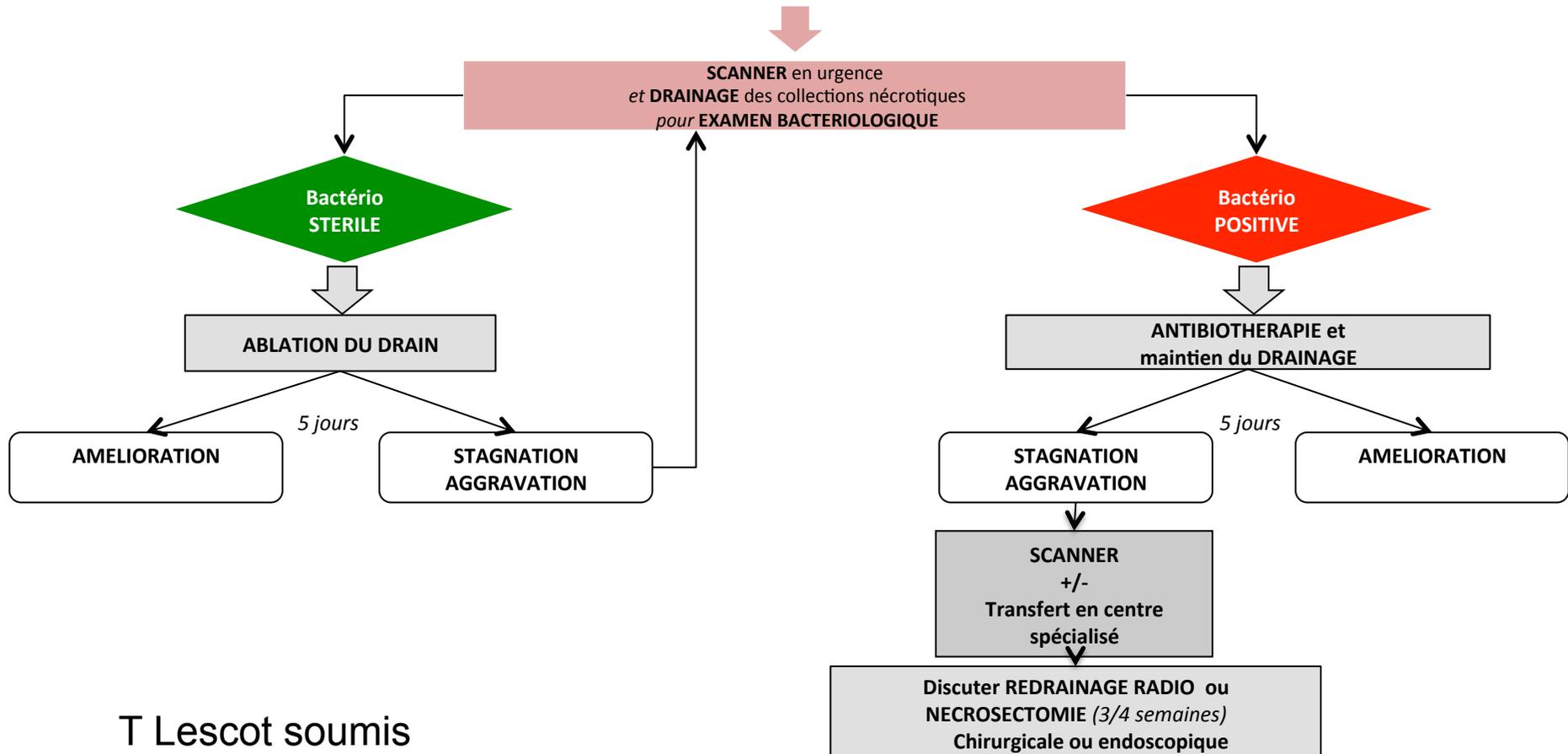
**BILAN SYSTEMATIQUE**  
 TDM dans les 48 heures  
 Echographie abdominale dans les 48 heures  
 Bilan lipidique à l'admission

**ALIMENTATION ET NUTRITION**  
 nutrition entérale continue dès J3-J5  
 25-30 kcal/kg/jour  
 Nutrition parentérale:  
 - Si intolérance à la NE  
 - Si besoins énergétiques non couverts à J5-J7

**DEFAILLANCE D'ORGANES**  
 Admission en unité de soins aigus  
 Monitoring de la pression intra-abdominale

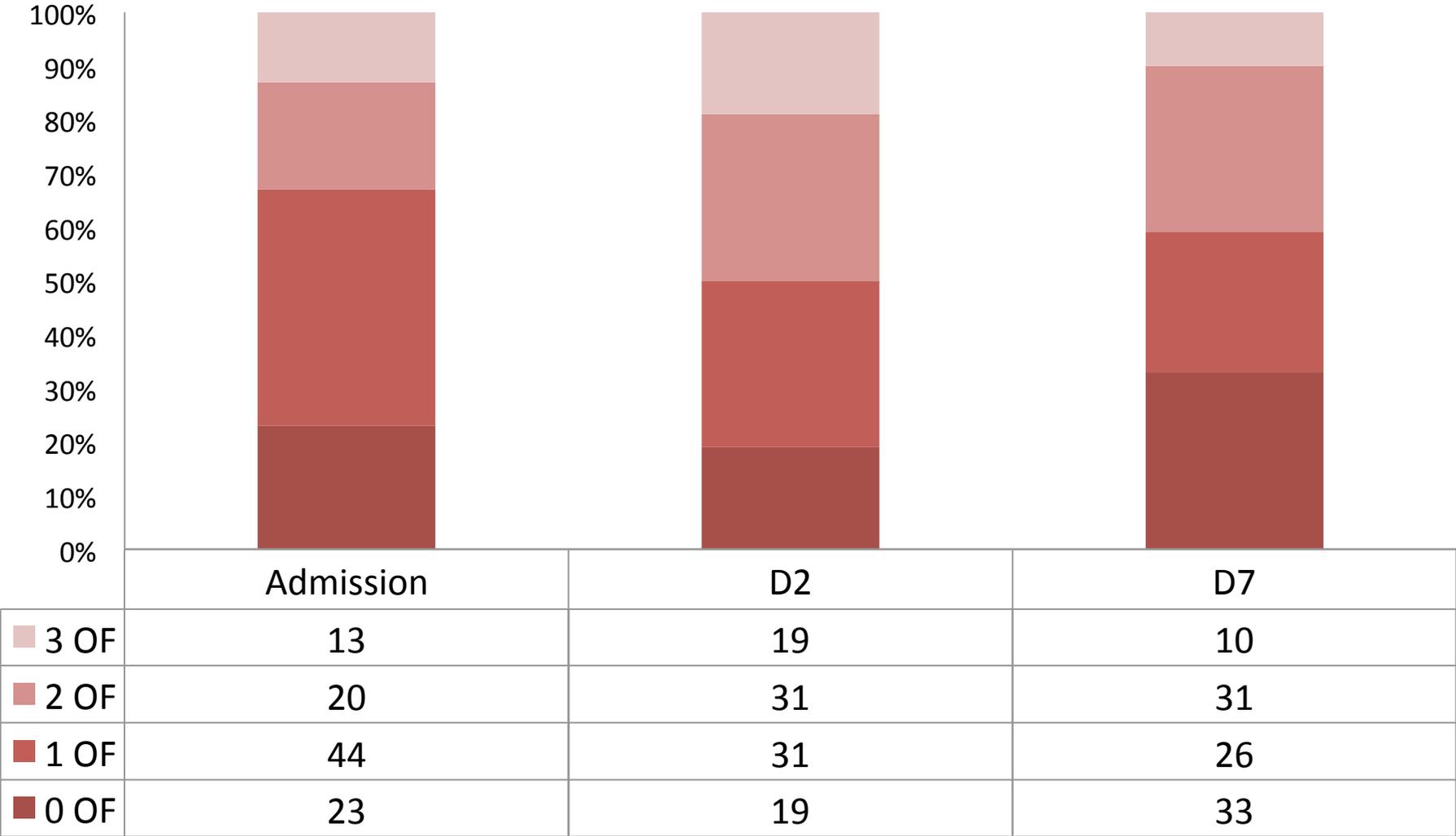
**INDICATIONS CHIRURGICALES**  
 Syndrome du compartiment abdominal  
 Suspicion d'ischémie digestive  
 Suspicion de perforation digestive  
 Hémorragie digestive non traitable (endoscopiquement ou radiologiquement)

**SUSPICION D'INFECTION DE NECROSE**  
*Hyperleucocytose/fièvre/absence d'amélioration ou aggravation des défaillances d'organes/ bulles gazeuses intra-nécrotiques au scanner*



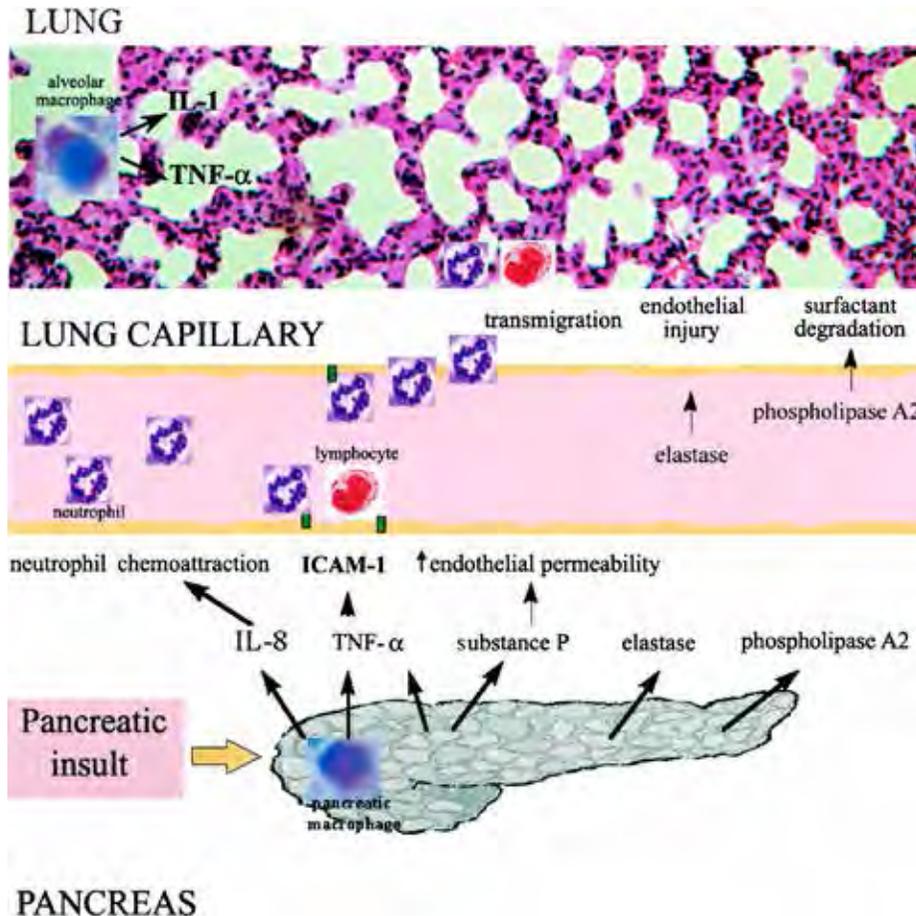
T Lescot soumis

# Evolution par nombre de défaillances



■ 0 OF ■ 1 OF ■ 2 OF ■ 3 OF

# Défaillance respiratoire



Dysfonction diaphragmatique

Epanchement pleuraux

SDRA ( $\approx 10\%$ )

Infections

Pastor C M et al. Chest 2003;124:2341-2351



# Determinant-Based Classification of Acute Pancreatitis Severity

## *An International Multidisciplinary Consultation*

*E. Patchen Dellinger, MD,† Christopher E. Forsmark, MD,‡ Peter Layer, MD, PhD,§ Philippe Lévy, MD,|| Enrique Maraví-Poma, MD, PhD,¶ Maxim S. Petrov, MD, MPH, PhD,# Tooru Shimosegawa, MD, PhD,\*\* Ajith K. Siriwardena, MD,†† Generoso Uomo, MD,‡‡ David C. Whitcomb, MD, PhD,§§ and John A. Windsor, MBChB, MD, FRACS#; on behalf of the Pancreatitis Across Nations Clinical Research and Education Alliance (PANCREA)*

Annals of surgery 2012

	Mild AP	Moderate AP	Severe AP	Critical AP
(Peri)pancreatic necrosis	No	Sterile	Infected	Infected
	AND	AND/OR	OR	AND
Organ failure	No	Transient	Persistent	Persistent

Dysfonction d'organe: SOFA (rénale, hémodynamique, respiratoire)  $\geq 2$   
 Transitoire si durée < 48 heures

# Performance of the revised Atlanta and determinant-based classifications for severity in acute pancreatitis

S. S. Bansal<sup>1</sup>, J. Hodson<sup>2</sup>, R. S. Sutcliffe<sup>1</sup>, R. Marudanayagam<sup>1</sup>, P. Muiesan<sup>1</sup>, D. F. Mirza<sup>1</sup>, J. Isaac<sup>1</sup> and K. J. Roberts<sup>1</sup>

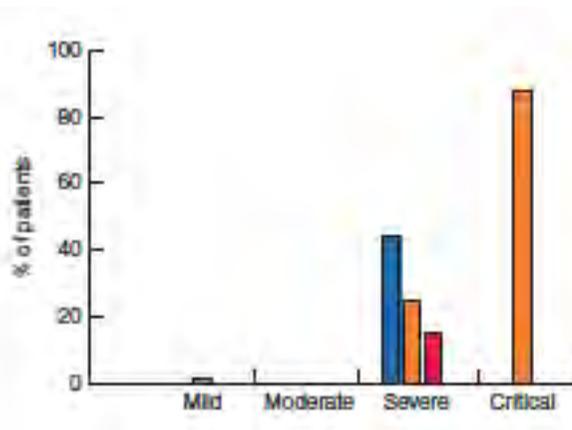
Departments of <sup>1</sup>Pancreatic Surgery and <sup>2</sup>Statistics, University Hospitals Birmingham NHS Trust, Birmingham, UK  
 Correspondence to: Mr K. J. Roberts, Department of Pancreatic Surgery, University Hospitals Birmingham NHS Trust, Birmingham B15 2TH, UK  
 (e-mail: j.k.roberts@bham.ac.uk)

*British Journal Surgery 2016*

228 patients

DBC Vs ATLANTA

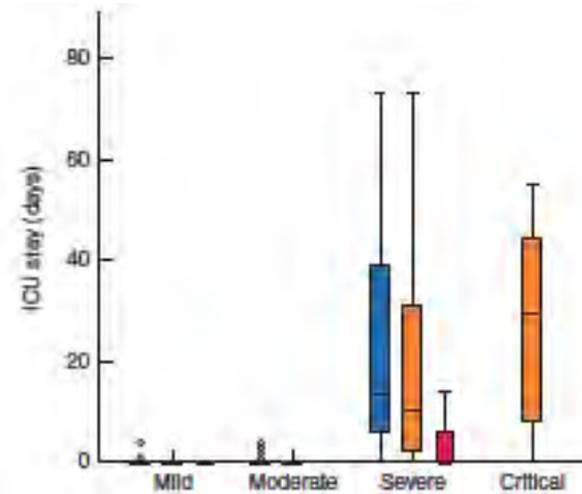
Mortalité



0,931

0,955

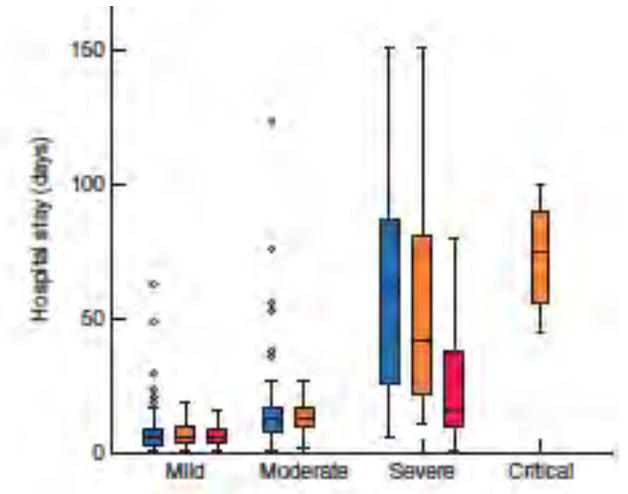
Durée de séjour réa



0,673

0,637

Durée de séjour H



0,635

0,648

# Comparison Between Revised Atlanta Classification and Determinant-Based Classification for Acute Pancreatitis in Intensive Care Medicine. Why Do Not Use a Modified Determinant-Based Classification?

Felix Zubia-Olaskoaga, MD, PhD<sup>1</sup>; Enrique Maravi-Poma, MD, PhD<sup>2</sup>; Iratxe Urreta-Barallobre, MD<sup>3</sup>; María-Rosario Ramírez-Puerta, MD<sup>4</sup>; Mónica Mourelo-Fariña, MD<sup>5</sup>; María-Pilar Marcos-Neira, MD, PhD<sup>6</sup>; in representation of the Epidemiology of Acute Pancreatitis in Intensive Care Medicine Study Group

CCM 2016

Revised Atlanta Classification	Moderately severe		Severe	
Determinant-Based Classification	Moderate	Severe		Critical
Modified Determinant-Based Classification	Transient OF without IN (LC)	Transient OF with IN (LC)	Persistent OF without IN (LC)	Persistent OF with IN (LC)

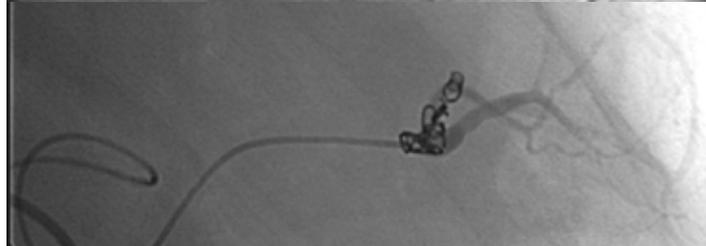
Classifications	OR (95% CI)	
	Mortality	Morbidity
Modified Determinant-Based Classification (reference group 1)		
Group 2	3.09 (0.49–19.39)	27.16 (9.27–79.55)
Group 3	30.69 (9.25–101.85)	1.60 (0.52–4.95)
Group 4	62.59 (18.46–212.20)	140.57 (38.75–509.94)
AUC (95% CI)	0.81 (0.77–0.85)	0.80 (0.73–0.86)
Revised Atlanta Classification (reference moderate-severe)		
Severe	30.14 (11.89–76.41)	3.03 (1.68–5.45)
AUC (95% CI)	0.77 (0.73–0.81)	0.64 (0.57–0.70)
Determinant-Based Classification (reference moderate)		
Severe	22.78 (8.03–64.64)	2.95 (1.34–6.49)
Critical	40.18 (13.41–120.36)	176.14 (37.12–835.76)
AUC (95% CI)	0.77 (0.72–0.81)	0.81 (0.74–0.88)

# Complications locorégionales des formes nécrosantes

- Complications vasculaires
- Complications Digestives  
=> Perforation d'organe creux
- Complications infectieuses

# Complications vasculaires

## Faux anévrisme



## Thrombose veineuse





# Antibiotic therapy for prophylaxis against infection of pancreatic necrosis in acute pancreatitis (Review)

Villatoro E, Mulla M, Larvin M

7 essais, 400 patients

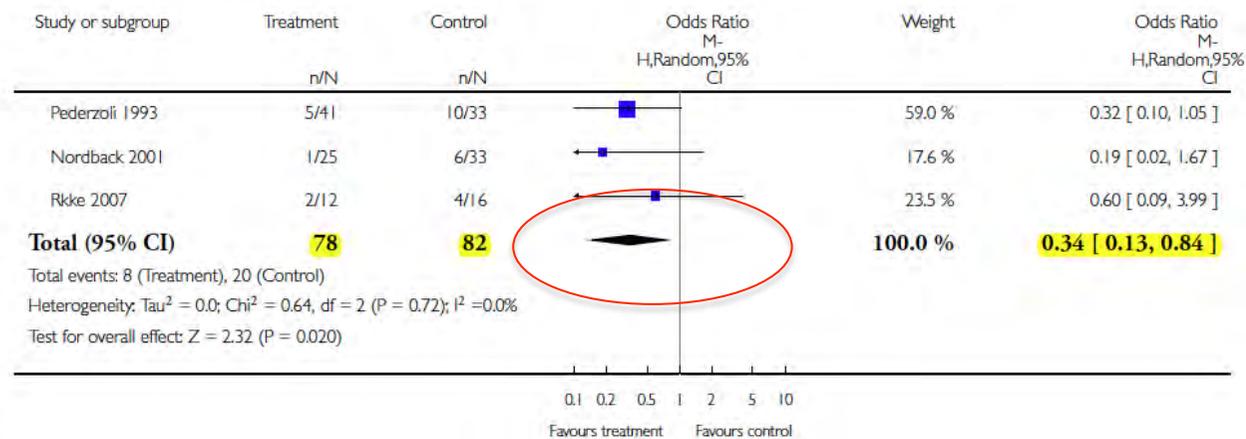
Pas d'effet significatif sur la mortalité, infections de nécrose, infections systémiques ou fongiques

## Analysis 4.2. Comparison 4 Imipenem versus control, Outcome 2 Infected Pancreatic Necrosis (imipenem).

Review: Antibiotic therapy for prophylaxis against infection of pancreatic necrosis in acute pancreatitis

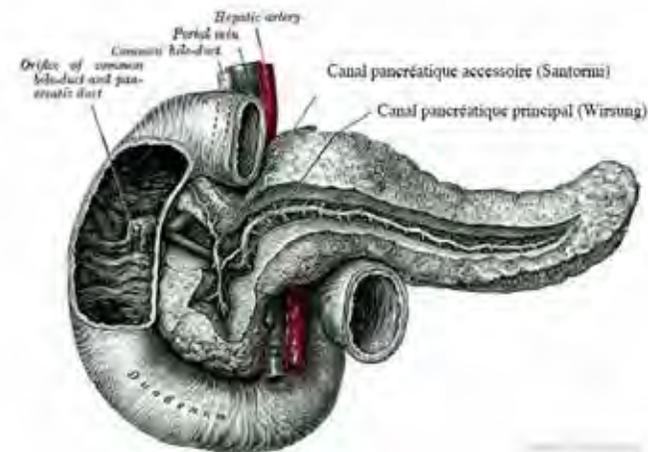
Comparison: 4 Imipenem versus control

Outcome: 2 Infected Pancreatic Necrosis (imipenem)



# Pancréas

- « Tout en viande » (*pan; kreas*)
- Organe rétropéritonéale, sus mésocolique
- 15 x 6 x 3 cm => 80 grammes
- Tête – isthme - corps - queue
- Glande
  - Fonction Endocrine ( $\alpha$ , *glucagon*;  $\beta$ , *insuline*;...)
  - Fonction Exocrine

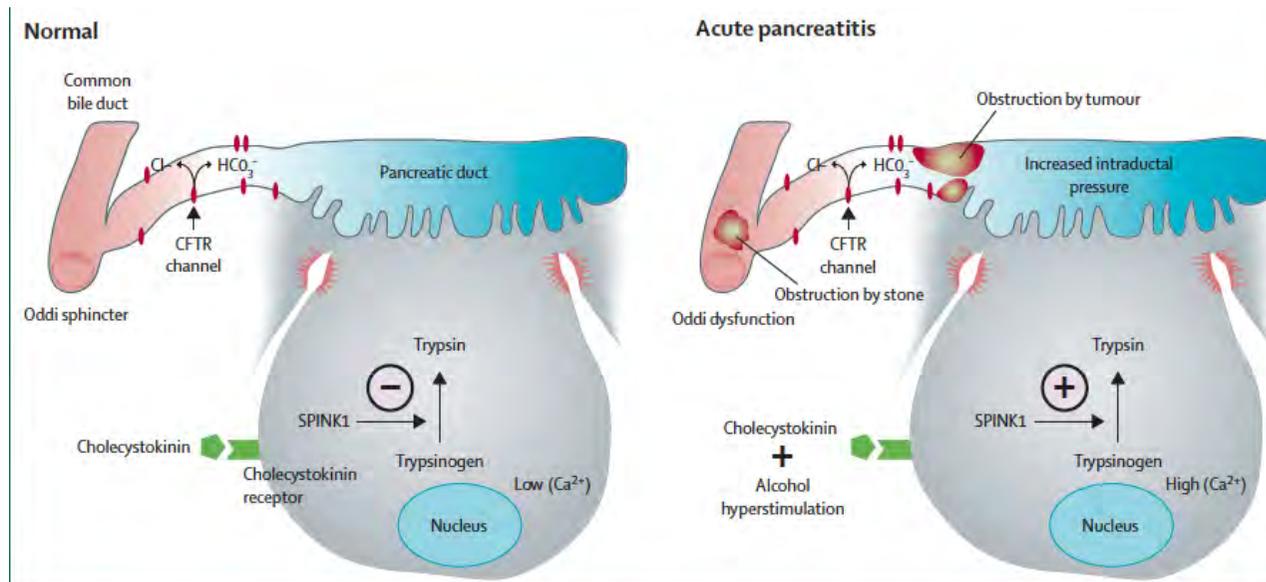


# Pancréatite aigüe

Activation anormale du trypsinogène en trypsine active

« Autodigestion » de la glande

Processus inflammatoire responsable d'une réaction inflammatoire locale et systémique



# Pancr atite aig e

- **2 crit res parmi**
  - Douleur abdominale  vocatrice
  - Lipas mie (amylas mie) > 3N
  - Aspect scanographique compatible
  
- 11 000 cas annuels
  
- 60% d'hommes, cinquantaine
  
- Maladie alcoolique + lithiasique biliaire = 80   90% des cas
  
- 2% des patients admis en r animation / USC

*Banks PA et al., Gut 2013*

*JUNG B et al., Annales Fran aises d'Anesth sie et de R animation, 2011*