Management of infection in severe acute pancreatitis BVIKM/SBIMC 2011

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- Relevance of pancreatitis and of infections in SAP
- Mechanism for infection of pancreatic necrosis
- Type and timing of infections
- Predicting and diagnosing IPN
- Preventing infections in SAP
- Treating infections in SAP
- ERCP, percutaneous drainage and surgery

Relevance of acute pancreatitis

Acute pancreatitis

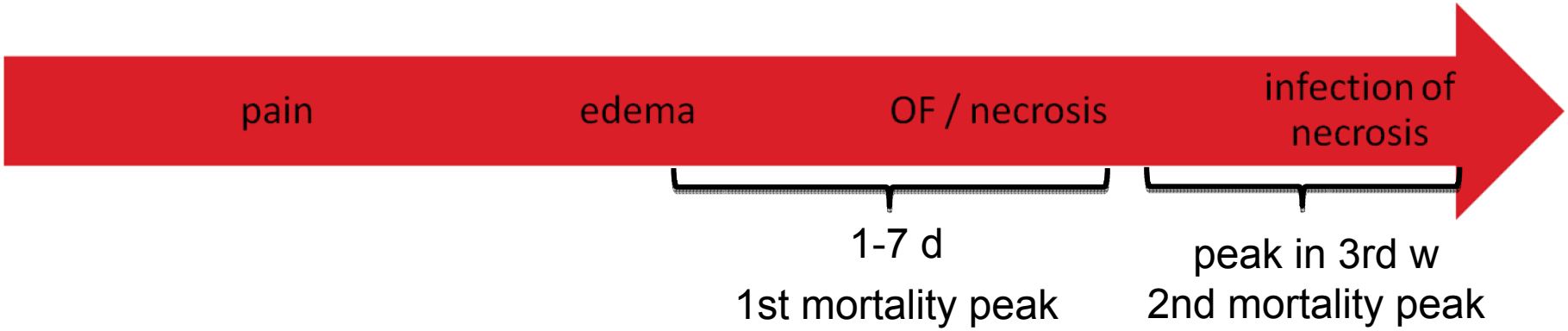
incidence of first attack = 5-80/100000

mild = 70-90%

severe (OF or PN) = 10-30%

mortality <1%

mortality 10 - 40 %



Relevance of infection in acute pancreatitis

Mortality associated with infected pancreatic necrosis (IPN) compared with no IPN in patients with organ failure (OF).

- 1478 patients with acute pancreatitis
- Mortality with IPN but no OF = 11%
- Mortality with OF but no IPN = 22%
- Mortality with OF + IPN = 43%

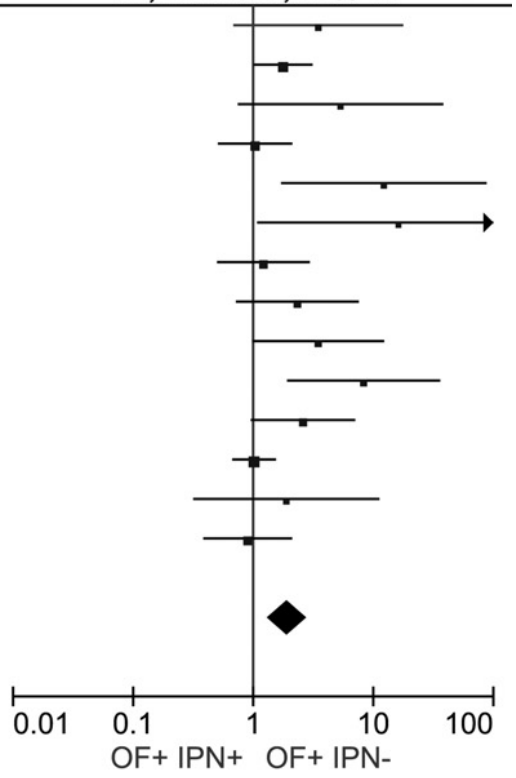
Petrov MS. Organ failure and infection of pancreatic necrosis as determinants of mortality in patients with acute pancreatitis. Gastroenterology 2010

Forest plot for mortality associated with infected pancreatic necrosis (IPN) compared with no IPN in patients with organ failure (OF). CI, confidence interval

Study or Subgroup	OF+ IPN+ Events	OF+ IPN+ Total	OF+ IPN- Events	OF+ IPN- Total	Weight	Risk ratio IV, Random, 95% CI
Buchler et al.	4	27	2	47	4.3%	3.48 [0.68, 17.77]
Garg et al.	15	19	8	18	13.1%	1.78 [1.01, 3.13]
Le Mee et al.	9	27	1	16	3.1%	5.33 [0.74, 38.29]
Lutfarakhmanov et al.	8	18	9	21	11.2%	1.04 [0.51, 2.12]
Lytras et al.	7	12	1	21	3.1%	12.25 [1.71, 87.98]
Pellegrini et al.	4	4	0	8	1.8%	16.20 [1.08, 243.36]
Perez et al.	7	23	7	28	9.2%	1.22 [0.50, 2.97]
Radenkovich et al.	5	10	3	14	6.7%	2.33 [0.72, 7.59]
Rau et al.	3	10	5	58	6.1%	3.48 [0.98, 12.32]
Remes-Troche et al.	6	13	2	36	5.0%	8.31 [1.91, 36.11]
Rocha et al.	5	10	5	26	8.1%	2.60 [0.95, 7.08]
Sharma et al.	14	26	36	68	15.0%	1.02 [0.67, 1.55]
Tenner et al.	2	9	2	17	3.7%	1.89 [0.32, 11.26]
Tireli et al.	3	5	6	9	9.6%	0.90 [0.38, 2.11]
Total (95% CI)		**213**		**387**	**100.0%**	**1.94 [1.32, 2.85]**
Total events	92		87			

Heterogeneity: Tau² = 0.21; Chi² = 24.82, df = 13 (*P* =.02); I² = 48%

Test for overall effect: Z = 3.39 (*P* =.0007)

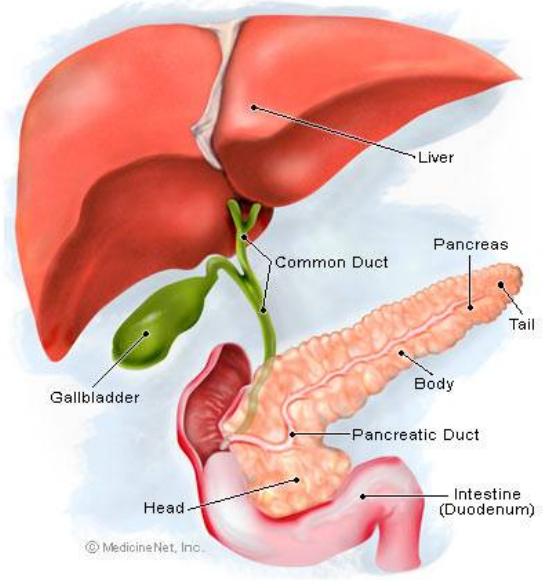


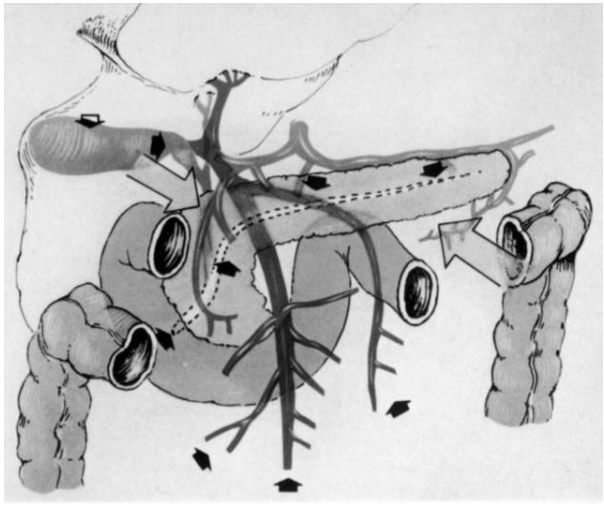
Petrov MS. Organ failure and infection of pancreatic necrosis as determinants of mortality in patients with acute pancreatitis. Gastroenterology 2010

Mechanism of infection of pancreatic necrosis: which route?

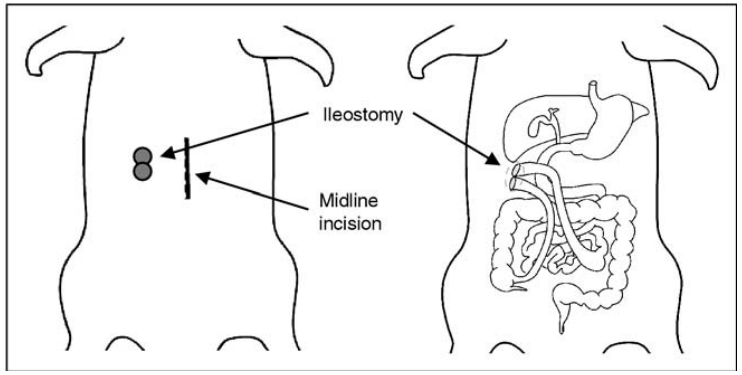
Bacterial translocation: transmural migration via the wall of the intestine

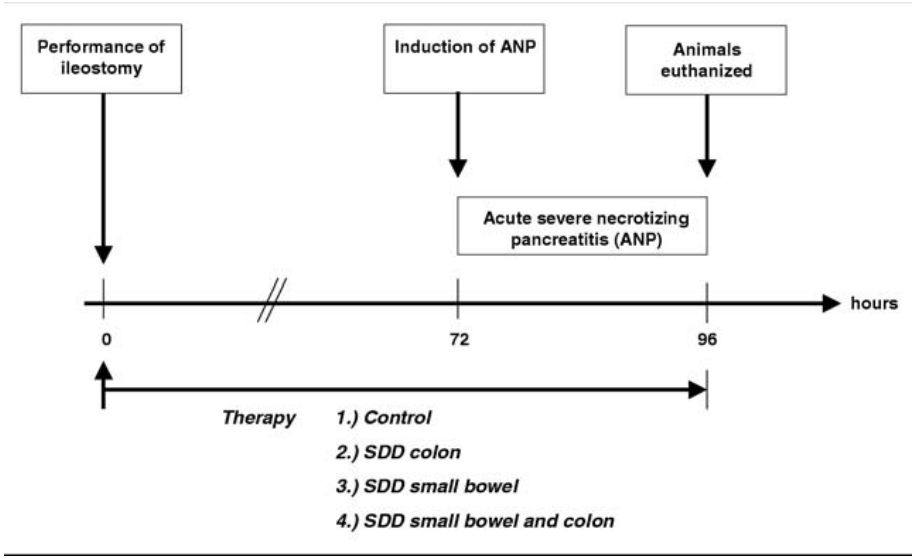
- hematogenous via de circulation
- via ascites to the pancreas
- via lymphatics to the circulation
- via the biliary duct or from the duodenum

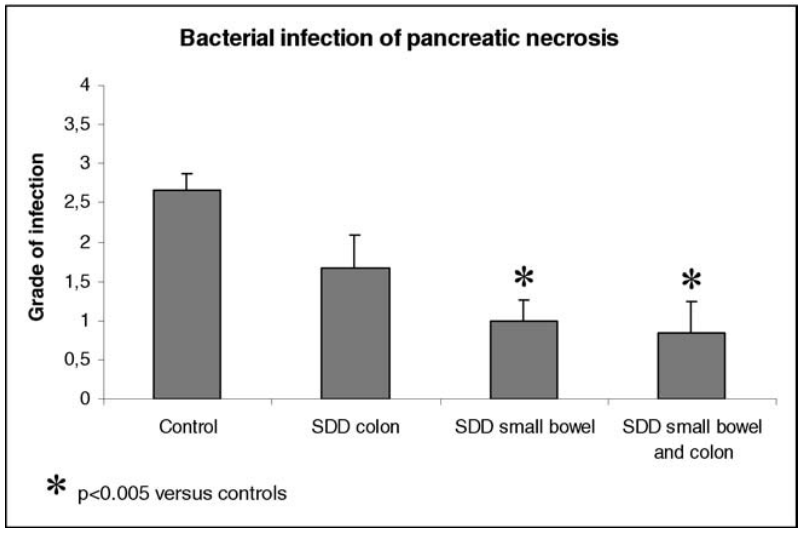




Mechanism of infection (2)

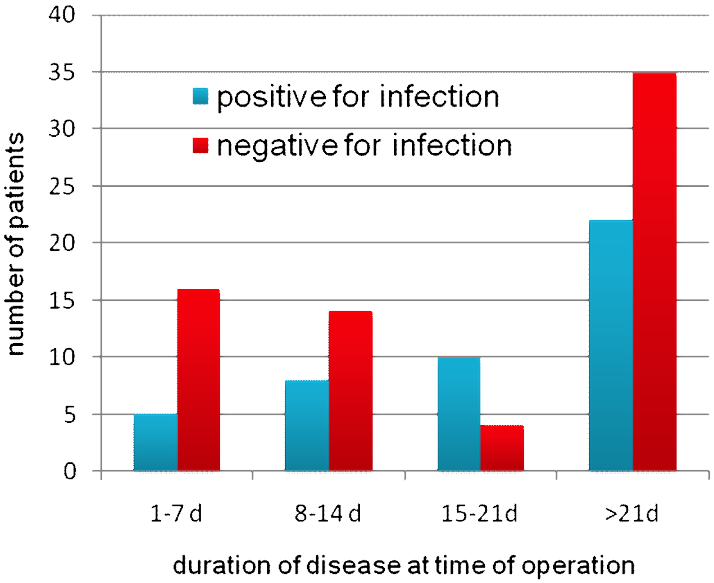


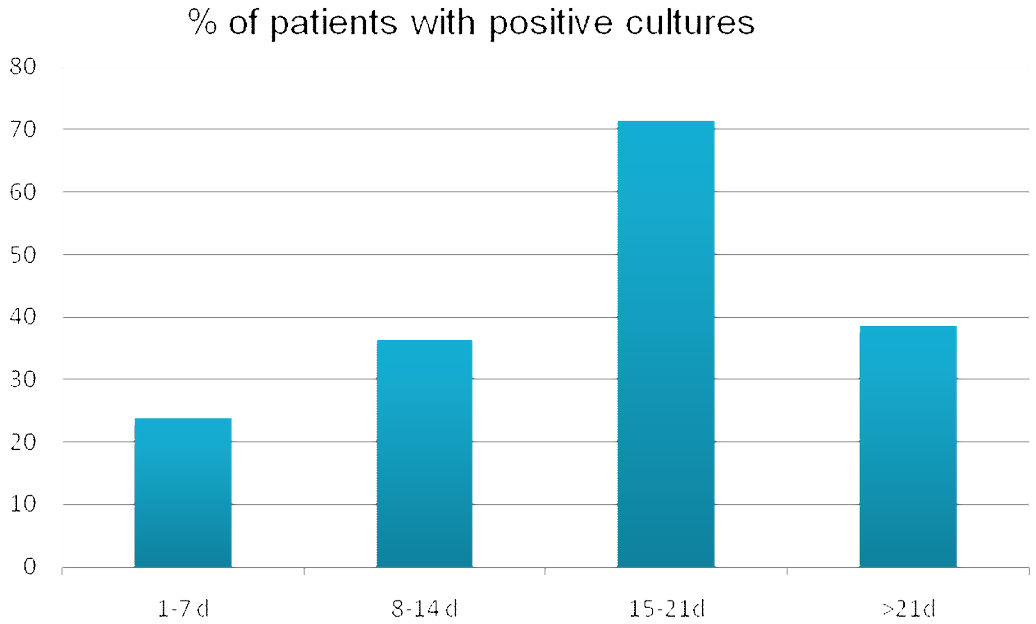




Fritz S. et al: Bacterial translocation and infected pancreatic necrosis in acute necrotizing pancreatitis derives from small bowel rather than from colon. Am J Surgery 2010

Timing of pancreatic infection (1)





Beger HG et al: Gastroenterology 1986, n=114, cultures taken during surgery were positive in 45 = 39,5%

Timing of pancreatic infection (2)

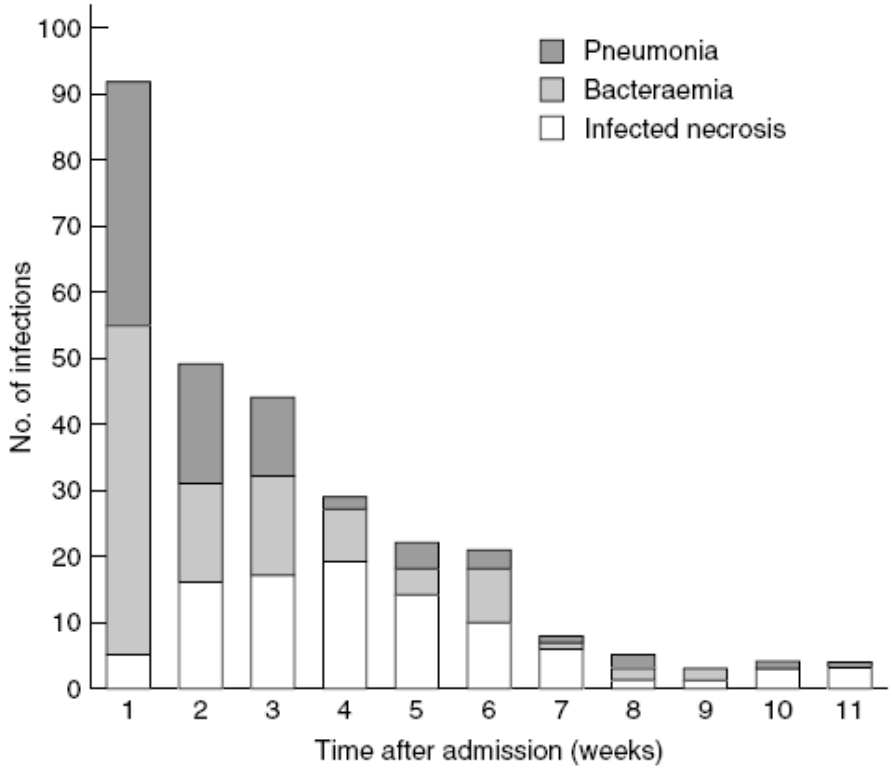


Fig. 1 Time of diagnosis of pneumonia, bacteraemia and infected necrosis in 173 patients during a first episode of acute pancreatitis. A patient with more than one separate infection may be depicted several times (for example bacteraemia in week 1 and infected necrosis in week 4), but only the initial infection is listed if there were multiple infections of the same type (such as bacteraemia in week 1 and in week 3)

Median time to diagnosis of first infection

= 8 d (IQR 3-20)

For bacteremia = 7 d

For pneumonia = 7d

For IPN = 26 d

Besselink MG et al. Timing and impact of infections in acute pancreatitis. Br J Surg 2009 (cohort study, n = 731, infection = 173).

Table 4 Pathogens cultured from initial infectious complications in 173 patients

	No. of patients
Gram-positive bacteria	
Staphylococcus spp.	64
Staphylococcus aureus	37
Coagulase-negative *Staphylococcus*	23
Enterococcus spp.	29
Streptococcus spp.	16
Other Gram-positive microorganisms	9
Gram-negative bacteria	
Enterobacteriaceae	86
Escherichia coli	48
Klebsiella spp.	20
Other Gram-negative microorganisms	26
Fungi	20
Candida spp.	16

Gram pos = ± 50%
Gram neg = ± 50%
Candida = 5-37%

Besselink MG et al. Timing and impact of infections in acute pancreatitis. Br J Surg 2009 (n = 731, infection = 173).

Relevance of intra-abdominal fungal infections (IFI) in SAP: as compared to IBI: more morbidity, idem mortality

Table 4. Published mortality outcomes of intra-abdominal fungal infections in SAP

Series	Study period	Number	In-hospital mortality (%)	Comments
This study (Vege *et al.*)	1992–2001	30	20	No difference in IFI and IBI mortality rate
Berzin *et al.* (8)	2000–04	7	0	All patients had secondary infection
Chakrabarti *et al.* (15)	2000–03	17	41	Decreased mortality in IFI vs. to those without *candida* infection (53%)
King *et al.* (14)	1992–2001	5	0	No difference in IFI and IBI mortality rate
Connor *et al.* (11)	1996–2003	21	48	Increased mortality in IFI (83%) compared to those without *candida* infection (28%)
De Waele *et al.* (13)	1995–2002	17	35	No mortality difference between patients with and without IFI
Isenmann *et al.* (6)	1982–97	22	64	Increased mortality in IFI vs. IBI (19%)
Gloor *et al.* (12)	1994–2000	8	25	No difference in IFI and IBI (20%) mortality rate
Gotzinger *et al.* (10)	1986–98	22	84	Increased mortality in IFI (84%) compared WITH those without *candida* infection (32%)
Grewe *et al.* (16)	1983–95	7	43	Increased mortality in IFI vs. IBI (20%)
Hoerauf *et al.* (17)	1987–93	13	54	Increased mortality in IFI vs. IBI (14%)
Aloia *et al.* (18)	1986–93	17	18	No comparison group

IBI, intra-abdominal bacterial infection; IFI, intra-abdominal fungal infection; NII, no intra-abdominal infection; SAP, severe acute pancreatitis.

Santhi Swaoop V et al. Outcomes of intra-abdominal fungal versus bacterial infections in SAP. Am J Gastroenterol 2009, n = 207, 30 with intra-abdominal fungal infection

Predicting pancreatic infection in SAP: procalcitonin

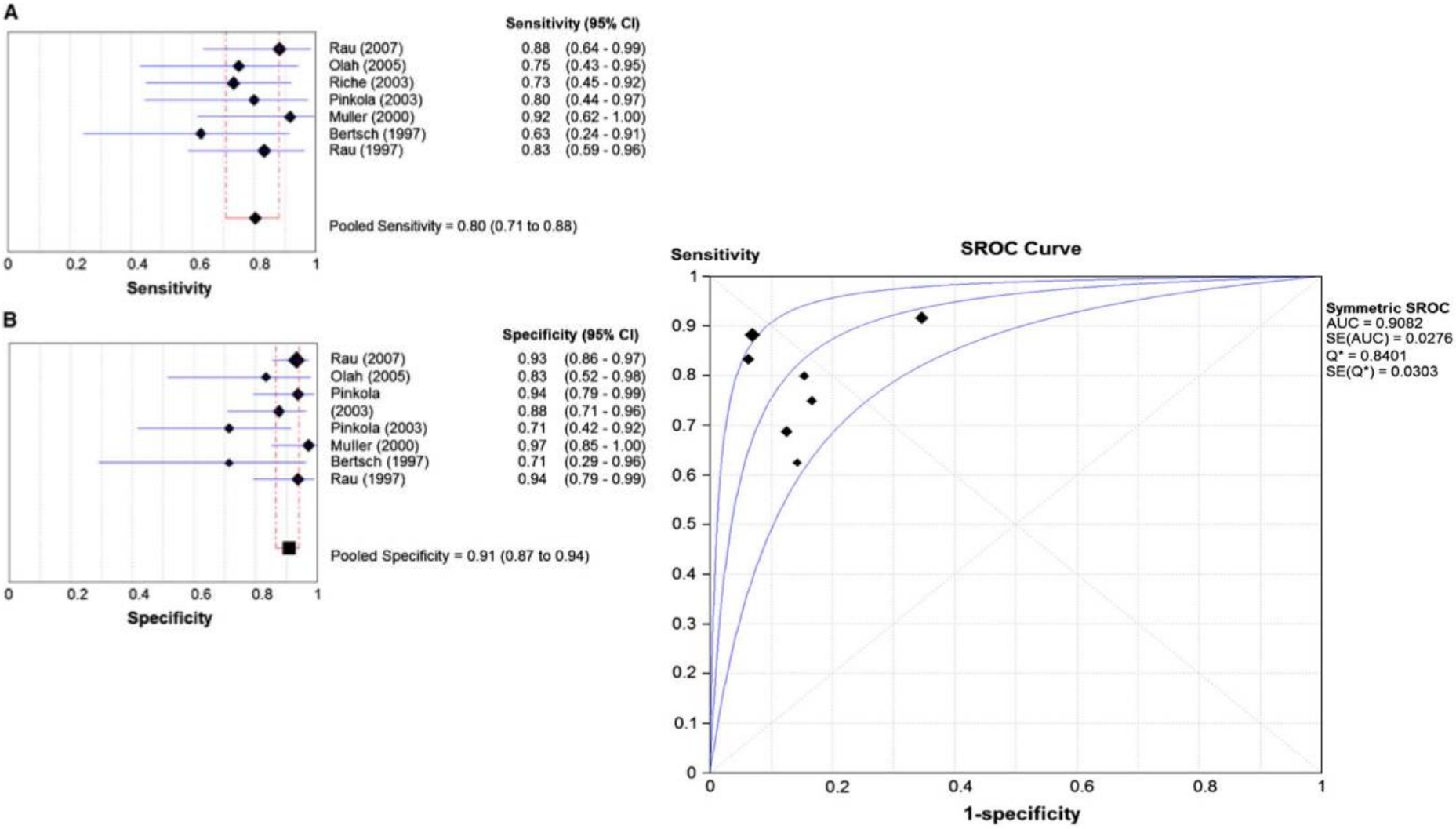
Table I. Technical characteristics of the included studies

Study (year)	*Study design*	*Evaluation*	*Time of blood samples*	*Method of PCT measurement*	*Time(s) of evaluation*	*Cutoff values for PCT (ng/mL)*
Rau et al[13] (1997)	Prospective	Mild vs SAP	Daily for 14 days	BRAHMS-IA	Highest value	1.8
Bertsch et al[37] (1997)	Prospective	Sterile vs IPN	Daily for 3 days	RIA	Highest value	0.5
Müller et al[33] (2000)	Prospective	Sterile vs IPN	Daily for 14 days	BRAHMS-IA	Highest value	0.48
Mandi et al[14] (2000)	Prospective	Mild vs SAP	Daily for 14 days	BRAHMS-IA	48 h	1.2
Pindak et al[38] (2000)	Prospective	Mild vs SAP	Admission+ day 1	BRAHMS-IA	Highest value	0.5
Pezzilli et al[34] (2000)	Prospective	Mild vs SAP	Daily for 5 days	BRAHMS-IA	—	0.25
Melzi D'Eril et al[35] (2000)	Prospective	Mild vs SAP	Day 1	BRAHMS-IA	Day 1	0.5
Frasquet et al[36] (2000)	Prospective	Mild vs SAP	Day 1	PCT-Q	Day 1	0.5
Kylanpaa-Back et al[18] (2001)	Prospective	Mild vs SAP	Day 1	BRAHMS-IA	Day 1	0.4
Kylanpaa-Back et al[19] (2001)	Prospective	Mild vs SAP	Daily for 2 days	PCT-Q	Day 1	0.5
Riche et al[15] (2003)	Prospective	Sterile vs IPN	Daily for 5 days	BRAHMS-IA	Highest value	2
Pinkola and Darvas[27] (2003)	Prospective	Sterile vs IPN	—	RIA	—	—
Ammori et al[17] (2003)	Prospective	Mild vs SAP	Admission	BRAHMS-IA	Admission	0.5
Olah et al[16] (2005)	Prospective	Sterile vs IPN	Daily for 3 days	PCT-Q	Highest value	0.5
Modrau et al[23] (2005)	Prospective	Mild vs SAP	Daily for 2 days	BRAHMS-IA	Admission +48 h	0.5-0.7
Bulbüller et al[26] (2006)	Prospective	Mild vs SAP	Daily for 14 days	BRAHMS-IA	48 h	0.5
Rau et al[20] (2007)	Prospective	Sterile vs IPN	Daily for 14 days	BRAHMS-IA	Highest value	3.5

BRAHMS-IA, BRAHMS immuno-luminometric assay; *IPN*, infected pancreatic necrosis; *PCT-Q*, procalcitonin strip test; *RIA*, radio immuno assay.

Mofidi R et al. The value of procalcitonin at predicting the severity of acute pancreatitis and development of infected pancreatic necrosis: Systematic review. Surgery 2009

Predicting pancreatic infection in SAP: procalcitonin



Mofidi R et al. The value of procalcitonin at predicting the severity of acute pancreatitis and development of infected pancreatic necrosis: Systematic review. Surgery 2009

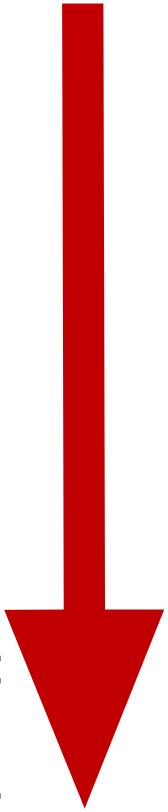
Diagnosing pancreatic infection in SAP

- surveillance cultures: no good data
- PCT: if >1.8 ng/ml on 2 consec. days: sens. 95%, specif. 88%, acc. 90%
- fine needle aspiration = FNA: sens. 91%, specif. 79%, acc. 84%
- surgery with cultures

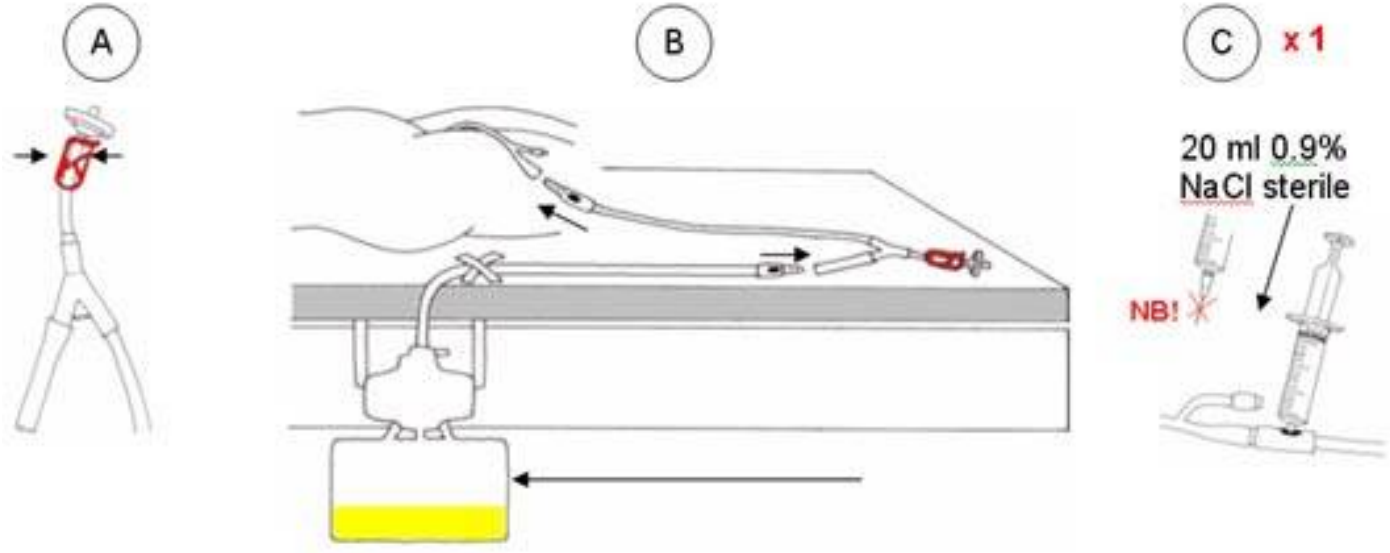
Rau B et al. The clinical value of procalcitonin in the prediction of infected necrosis in acute pancreatitis: Intensive Care Medicine 2000
Gerzof et al. Early diagnosis of pancreatic infection by computed tomography-guided aspiration. Gastroenterology 1987

Prevention of infection in SAP (1)
Intra-abdominal hypertension IAP values (mmHg)

- 0-5: normal range
- >12: raised = Intra-Abdominal Hypertension (IAH)
- >10: Cardiac output drops
- 3-13: normal postoperative range
- >15: compromised renal and splanchnic perfusion
- >15-20: increased airway pressures (PIP)
- >20-30: abdominal compartment syndrome (ACS) = emergency



Prevention of infection in SAP
(2)Prevalence of IAH in SAP



- Prevalence IAH 40%
- Prevalence ACS 10%

Leppäniemi A et al. Acta Clin Belg 2007; 62-suppl 1
Hou-Quan T et al. World J Gastroenterol 2004; 10: 919-921
De Waele J et al. Crit Care 2005; 9:R452-7
Hidalgo Rosas et al. Surgery 2006

Characteristic	IAH (n = 21)	Non-IAH (n = 6)	p-value
Pancreatic necrosis	20 (95%)	3 (50%)	0.025
Surgical management	9 (43%)	0 (0%)	0.070
Infected pancreatic necrosis	5 (24%)	0 (0%)	0.555
Organ dysfunction			
Pulmonary failure	20 (95%)	2 (33%)	0.004
Cardiovascular failure	19 (91%)	1 (17%)	0.001
Renal failure	18 (86%)	1 (17%)	0.004
LOS ICU (days)	21 (10–37)	3 (1–5)	0.003
LOS hospital (days)	42 (20–90)	12 (3–14)	0.015

Table 4 Comparison of complications and outcome between patients with and without ACS

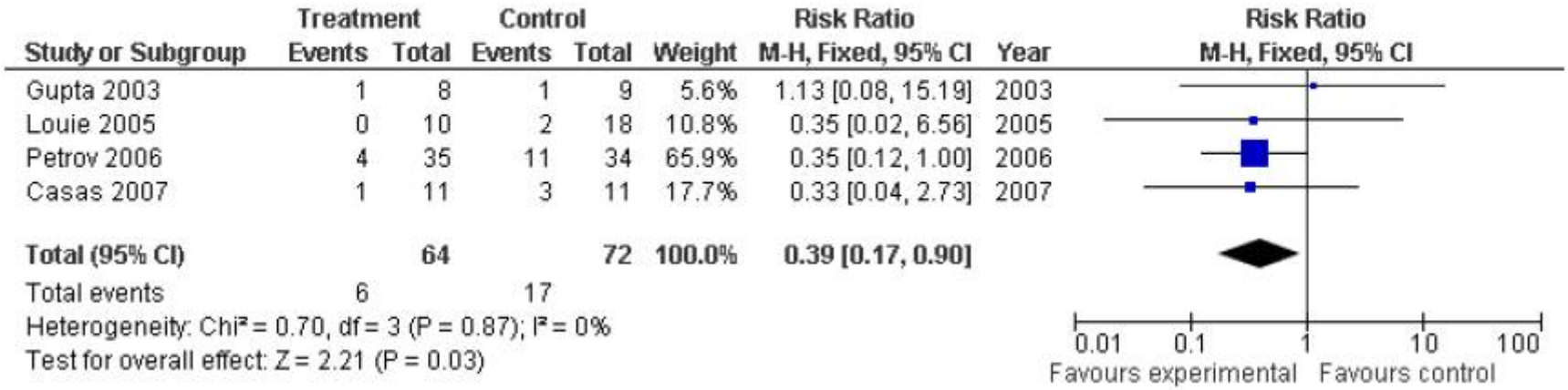
Complications and outcome	ACS (n = 20) (IAP > 20 mmHg)	IAH (n = 24) (12 mmHg ≤ IAP ≤ 20 mmHg)	Normal IAP (n = 30) (IAP < 12 mmHg)	χ^2 value	P value
Pancreatic infection (%)	12 (60.00)	2 (8.33)	2 (6.67)	23.84	< 0.001
Septic shock (%)	14 (70.00)	4 (16.67)	2 (6.67)	26.34	< 0.001
MODS (%)	18 (90.00)	10 (41.67)	7 (23.33)	21.85	< 0.001
In-hospital mortality (%)	15 (75.00)	1 (4.17)	1 (3.33)	41.93	< 0.001

De Waele J. Intra-abdominal hypertension in patients with severe acute pancreatitis. Crit Care 2005

Chen H et al . ACS in severe acute pancreatitis. World J Gastroenterol 2008

Prevention of infection in SAP (3)
Cochrane 2010: EN versus PN in SAP

Figure 14. Forest plot of comparison: 6 Enteral versus parenteral nutrition for acute pancreatitis, outcome: 6.2 Systemic infection in SAP.



Efficay factors for antibiotics in pancreatic tissue

Antibiotic	Panc. tissue conc after 120 min (mg/kg)	Efficacy factor
Imipenem	6	0.98
Quinolones (cipro or oflox)	0.9/1.7	0.86
Cephalosporines (cefotax)	9.1	0.78
Acylureidopenicillins (piperac)	20.3	0.72
Aminoglycosides (tobra)	0.4	0.22

Efficacy factor = type + frequency of bacteria, tissue concentrations, % of inhibition according to minimal inhibitory concentrations

Büchler M et al: Human pancreatic tissue concentrations of bactericidal antibiotics. Gastroenterol 1992 (n=89, only 8 with SAP)

Bassi C et al. Behavior of antibiotics in human necrotizing pancreatitis. Antimicrob agents Chemother 1994 (n=12)

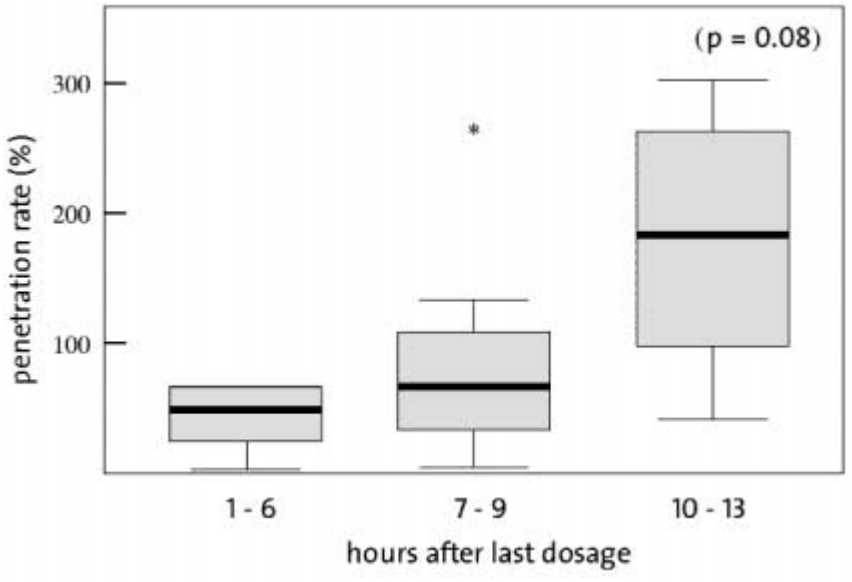


Figure 1. Box plot diagram showing median values; interquartile
ranges; total ranges of the penetration rate of ciprofloxacin into pancreatic necroses dependent on the duration of ciprofloxacin therapy (number of doses already given). Star represents extreme values. One extreme value of 868% in the third group is not shown in the figure.

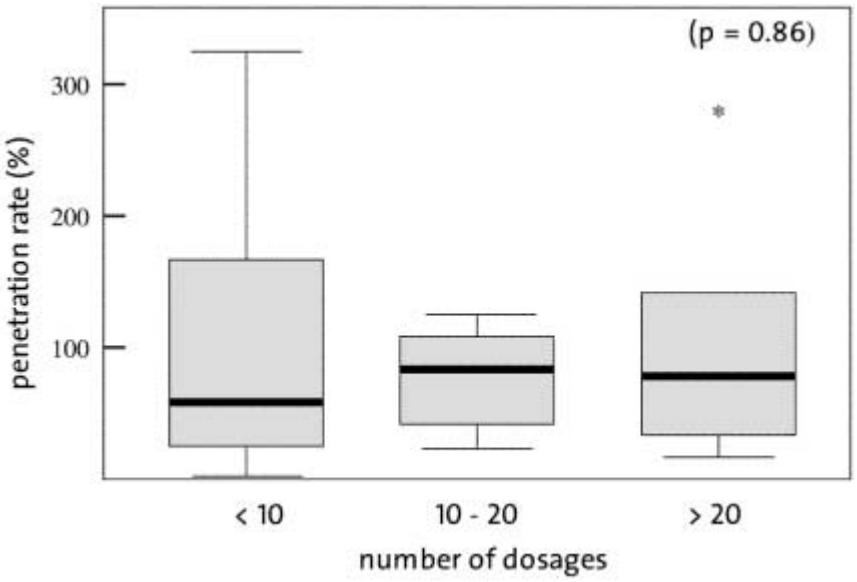


Figure 2. Box plot diagram showing median values; interquartile
ranges; total ranges of the penetration rate of ciprofloxacin into pancreatic necroses dependent on the dosage interval (12 or 24 h, respectively). Star represents extreme values. One extreme value of 868% in the first group is not shown in the figure.

U. Adam et al. Ciprofloxacin Penetration into Pancreatic Necroses. Infection 2001, (14 patients with 51 operations)

Randomized trials of AB prophylaxis AP

Study	Antibiotic scheme	Number of patients	Mortality (%)	Pancreatic infection (%)
Pederzoli et al. 1993	-Imipenem -No antibiotic	41 33	7 12	12 30
Sainio et al. 1995	-Cefuroxime -No antibiotic	30 30	3* 23	30 40
Schwarz et al. 1997	-Oflox+Metron -No antibiotic	13 13	0 15	62 54
Nordback et al. 2001	Imipenem No antibiotic	25 33	8 15	4 18
Luiten et al. 1995	-No antibiotic -SD + cefotax.	52 50	35% 22%*	38% 18%*

Santorini consensus document on acute pancreatitis.,Derveni et al. Intl. J of Pancreatology 1999. Guidelines for the management of acute pancreatitis., Toouli J et al: J Gastroenterol Hepatol 2002. The management of SAP: an evidenced-based review of the literature., Wyncoll DL: ICM 1999. UK guidelines for the management of acute pancreatitis ,BSG: GUT 1998. IAP guidelines for the surgical management of acute pancreatitis, Uhl et al: Pancreatology 2002.

Prophylactic antibiotic treatment in patients with predicted SAP: a placebo-controlled, double-blind trial.
Isenmann R et al. Gastroenterology 2004

	Intention-to-treat analysis, 114 patients		Necrotizing pancreatitis, 76 patients	
	Ciprofloxacin/ metronidazole, 58 patients	Placebo, 56 patients	Ciprofloxacin/ metronidazole, 41 patients	Placebo, 35 patients
Pulmonary insufficiency (%)	n = 26 (45)	n = 25 (45)	n = 21 (51)	n = 21 (60)
Renal insufficiency %)	n = 7 (12)	n = 8 (14)	n = 7 (17)	n = 7 (20)
Shock (%)	n = 5 (9)	n = 7 (13)	n = 5 (12)	n = 7 (20)
Mortality (%)	n = 3 (5)	n = 4 (7)	n = 3 (7)	n = 4 (11)
Surgical treatment (%)	n = 10 (17)	n = 6 (11)	n = 10 (24)	n = 6 (19)
Extrapancreatic infections (%)	n = 13 (22)	n = 13 (23)	n = 12 (29)	n = 12 (34)
Infected pancreatic necrosis (%)	n = 7 (12)	n = 5 (9)	n = 7 (17)	n = 5 (14)

Early antibiotic treatment for severe acute necrotizing pancreatitis: a randomized, double-blind, placebo-controlled study
Dellinger EP et al: Ann Surgery 2007

TABLE 2. Development and Time to Onset of Pancreatic or Peripancreatic Infection From Symptom Onset

	Treatment Group			
	Meropenem (n = 50)		Placebo (n = 50)	
	n	%	n	%
Patients with pancreatic or peripancreatic infection	9	18	6	12
Patients with resistant pancreatic or peripancreatic infection	4	8	3	6
Mean (range) no. of days to diagnosis of infection	21.3 (5–35)	—	20.8 (11–25)	

A double-blind, placebo-controlled trial of ciprofloxacin prophylaxis in patients with acute necrotizing pancreatitis
García-Barrasa A et al. J Gastrointest Surg 2009

	Group ciprofloxacin n=22 n (%)	Group placebo n=19 n (%)	p
Infected pancreatic necrosis	8 (36)	8 (42)	0.707
Number of patients with one or more extrapancreatic infections[a]	6 (27)	8 (42)	0.318
Pneumonia	0	2	
Urinary tract infection	3	3	
Central line infection	2	3	
Positive blood-culture	3	2	

[a] Some patients had two or more extrapancreatic infections

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

Villatoro E, Mulla M, Larvin M. *Cochrane Database of Systematic Reviews* 2010, Issue 5. Art. No.: CD002941. DOI: 10.1002/14651858.CD002941.pub3.

A previous version published in 2006 suggested a survival advantage overall, and a decrease in pancreatic infections for some types of antibiotic therapy (beta-lactam antibiotics). Since that review, two further studies have been published: both were double-blinded, randomised, clinical trials (RCTs). These studies have now been included and our conclusions have changed as a result.

In the current review, data were found and analysed from 7 trials involving 404 patients randomly allocated to receive antibiotics or placebo. Although death occurred less after antibiotics (8.4%) than placebo (14.4%), as did infected pancreatic necrosis (19.7% versus 24.4%) and other infections (23.7% versus 36%), the differences were not statistically significant and so genuine benefit cannot be confirmed. There were no major problems with antibiotic resistance, and fungal infections were similar (3.9% versus 5%). The quality of studies was variable and only two were 'blinded', whereby investigators and patients were unaware of which treatment patients received. Many different regimens were used, and of the two main types of antibiotics used, a beta-lactam appeared to work better. Only one type of antibiotic (imipenem) was considered on its own, showing a significant decrease in infection of the pancreatic necrosis.

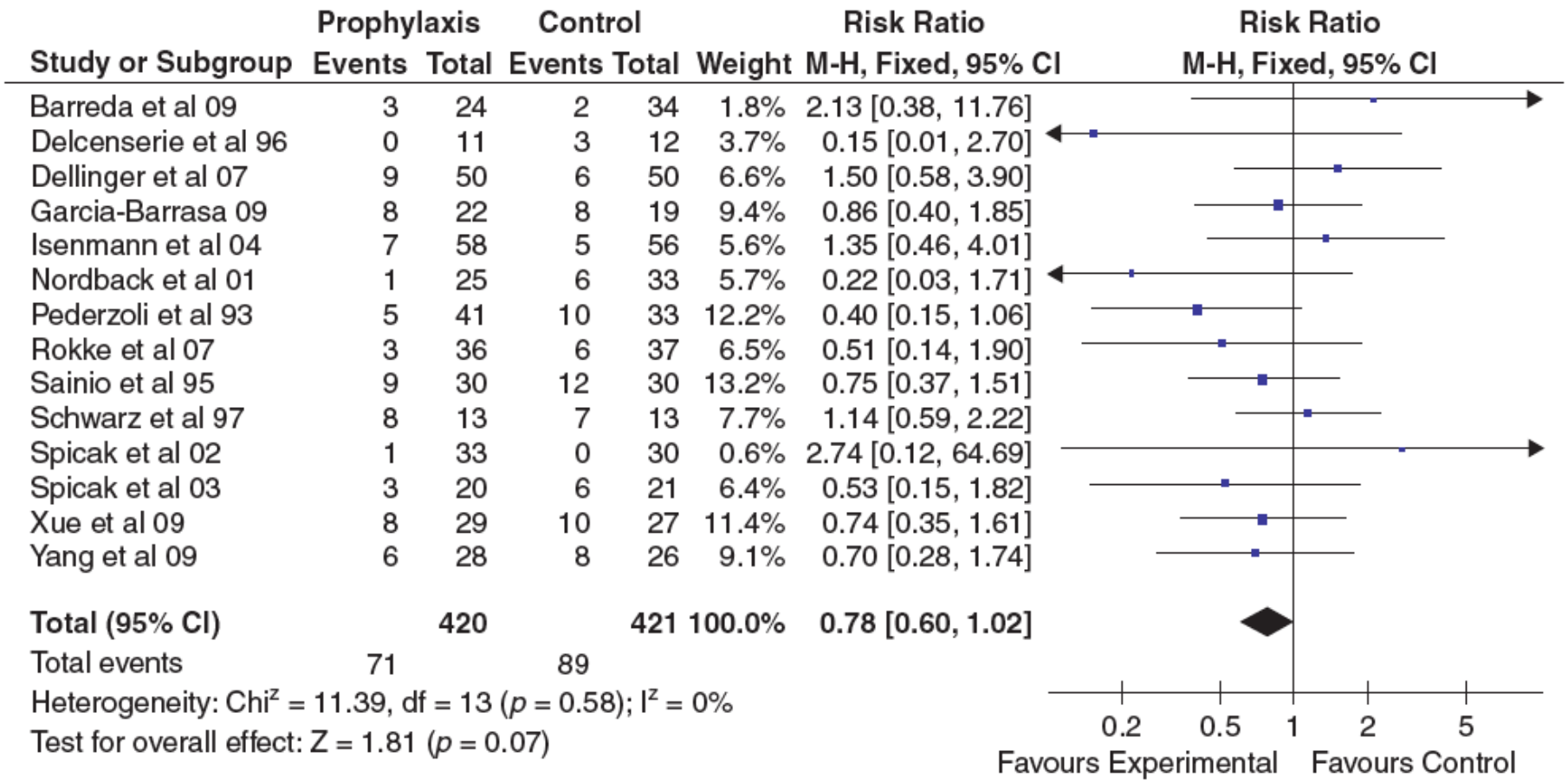
Although we cannot confirm benefit from the use of prophylactic antibiotics in this condition, consistent trends towards a beneficial effect nevertheless remain. Further, better designed studies, ideally with beta-lactam antibiotics, are required.

Wittau M et al. Systematic review and meta-analysis of antibiotic prophylaxis in severe acute pancreatitis. Scand J Gastroenterol 2011

Study/Author	Year	Adequate sequence generation	Concealed allocation	Blinding	Addressing incomplete outcome data	Free from selective outcome reporting
Pederzoli et al. [3]	1993	Yes	Unclear	No	Yes	Yes
Sainio et al. [4]	1995	Unclear	Yes	No	Yes	Yes
Delcenserie et al. [29]	1996	Yes	Unclear	No	Unclear	Yes
Schwarz et al. [30]	1997	Unclear	Unclear	No	Yes	Yes
Nordback et al. [31]	2001	Unclear	Unclear	No	Yes	Yes
Spicak et al. [32]	2002	No	Unclear	No	Unclear	Yes
Spicak et al. [33]	2003	Unclear	Unclear	No	Unclear	Yes
Isenmann et al. [1]	2004	Yes	Yes	Yes	Yes	Yes
Røkke et al. [27]	2007	Yes	Unclear	No	Yes	Yes
Dellinger et al. [5]	2007	Yes	Yes	Yes	Yes	Yes
Barreda et al. [34]	2009	Unclear	Unclear	No	Yes	Yes
Garcia-Barrasa et al. [6]	2009	Yes[#]	Yes[#]	Yes	Yes	Yes
Xue et al. [35]	2009	Yes	Unclear	No	Yes	Yes
Yang et al. [28]	2009	Yes	Unclear	No	Yes	Yes

[#]Details provided by author after personal communication (J. Busquets).

Forest plot of relative risk; [95% confidence intervals]: infected pancreatic necrosis



Wittau M et al. Systematic review and meta-analysis of antibiotic prophylaxis in severe acute pancreatitis. Scand J Gastroenterol 2011

SAP: when should we give antibiotics?

Prophylactic setting:

- Acute, mild pancreatitis = no
- Acute severe pancreatitis = no
- No prophylactic antifungal therapy
- SID: expectant position

Therapeutic setting:

- AB: yes before surgery or ERCP
- AB: yes, in case of infected necrosis
- carbapenem > other antibiotics
- treatment duration 2-4 (?) weeks

Nathens et al: CCM (Dec) 2004: Management of the critically ill patient with severe acute pancreatitis. Dellinger et al.

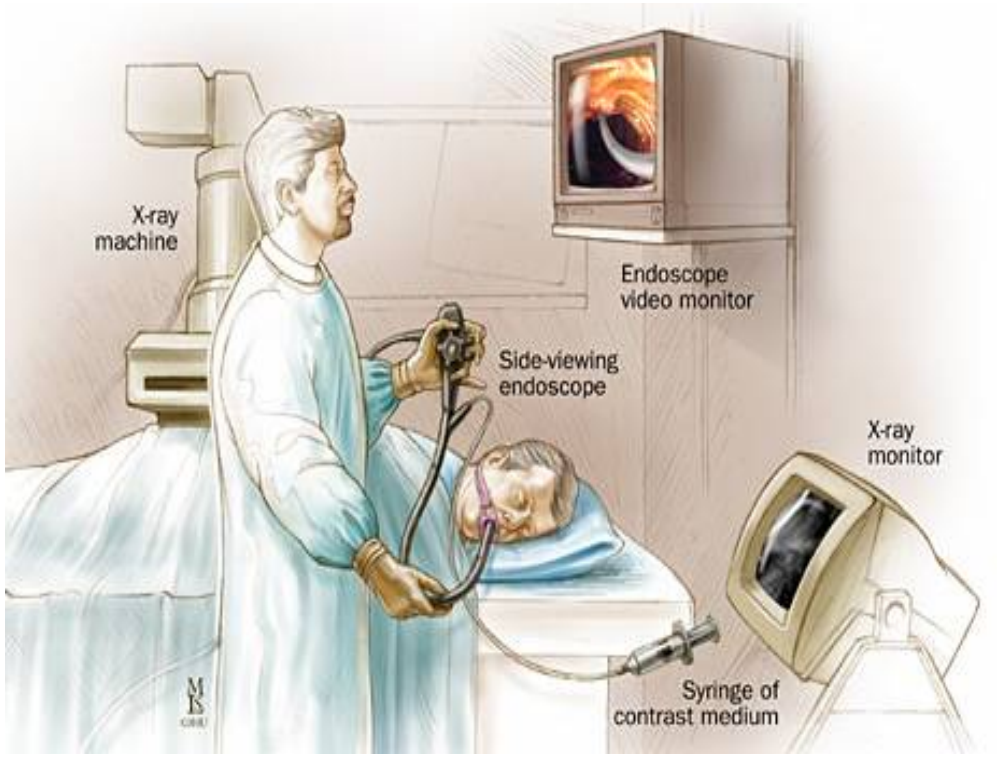
Annals of Surgery 2007;245:674-683

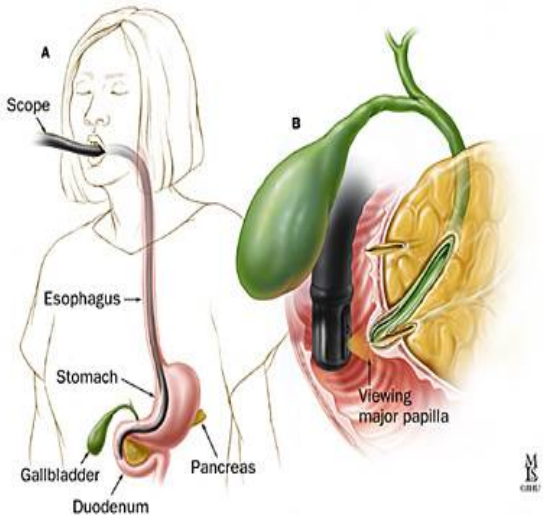
Banks PA. Practice guidelines in acute pancreatitis. Am J Gastroenterology 2006

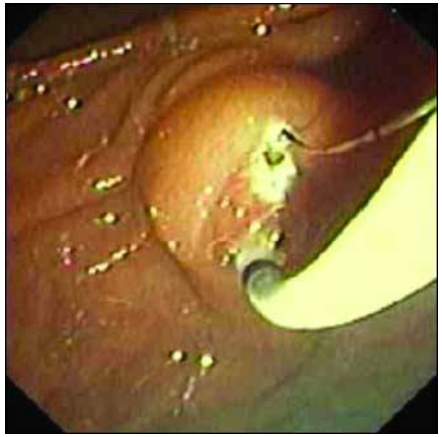
AGA Institute Medical Position Statement on Acute Pancreatitis. Gastroenterology 2007

Maravi-Poma E et al: early antibiotic treatment of septic complications in SAP: a prospective, randomized, multicenter study comparing two regimens with imipenem-cilastin. Intensive Care Med 2003

Endoscopic intervention in acute obstructive pancreatitis
Endoscopic retrograde cholangio-pancreaticograpy (ERCP)







Efficacy of biliary sfincterotomy in biliary pancreatitis?

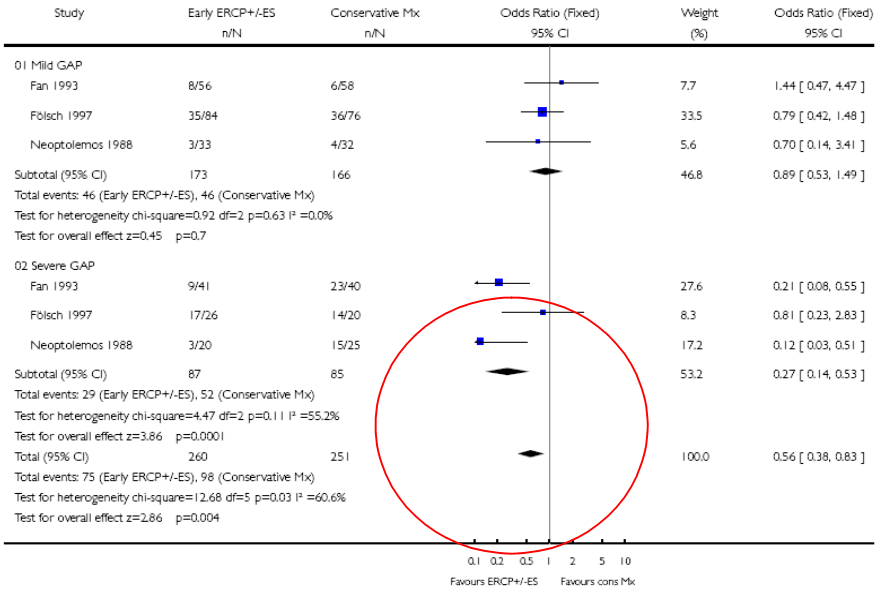
Auteur	Aantal (R/ vs co)	Tijd van interventie	Ernstige pancreatitis	ERCP succes	Morbiditeit	Mortality
Neoptolemos	121 (59/62)	< 72 hours	44%	88%	17 vs 34%	2 vs 8%
Fan	195 (97/98)	< 24 hours	42%	90%	16 vs 33%	2 vs 8%
Fölsch	238 (126/112)	< 72 hours	14%	96%	46 vs 51 %	11 vs 6 %
Nowak	238 (178/102)	< 24 hours	NR	NR	17 vs 36%	2 vs 13%

Neoptolemos J. Lancet 1988
Fan ST. NEJM 1993
Fölsch U. NEJM 1997
Nowak A. Gastroenterology 1995 (abstract)

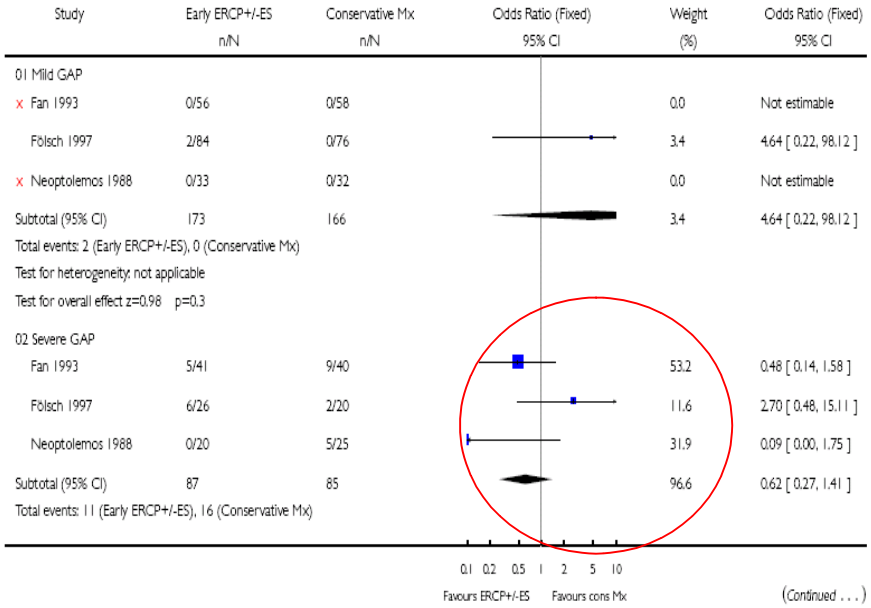
Efficacy of endoscopic intervention in biliary pancreatitis?

Meta-analysis – Ayub K. Cochrane Database Syst Rev. 2004

Complications



Mortality



…in SAP: ERCP only lowers morbidity…..current recommendation is: ERCP < 72 h

In case of cholangitis, CDL, persistent pijn, progressive LFT: earlier

Surgery for infected, necrotizing pancreatitis (PANTER study)

- Open necrosectomy: laparatomy with bilateral subcoastal incision + postop. lavage
- MISUA: PCD or ENDD ➔ 72 h 2nd drainage ➔ 72 h VARD with postop. lavage

Outcome	Minimally Invasive Step-up Approach (N=43)	Primary Open Necrosectomy (N=45)	Risk Ratio (95% CI)	P Value
Primary composite end point: major complications or death — no. (%)†	17 (40)	31 (69)	0.57 (0.38–0.87)	0.006
Secondary end points				
Major complication — no. (%)				
New-onset multiple-organ failure or systemic complications‡	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

Van Santvoort H et al. A step-up approach or open necrosectomy for necrotizing pancreatits. NEJM 2010, n=88

Surgery for infected, necrotizing pancreatitis (PANTER study)

	MiINV	OPNECR		
Total no. of operations¶				0.004
Per study group	53	91		
Range per patient	0–6	1–7		
Total no. of drainage procedures‖				<0.001
Per study group	82	32		
Range per patient	1–7	0–6		
New ICU admission at any time after first intervention — no. (%)**	7 (16)	18 (40)	0.41 (0.19–0.88)	0.01
Days in ICU				0.26
Median	9	11		
Range	0–281	0–111		
Days in hospital				0.53
Median	50	60		
Range	1–287	1–247		

Van Santvoort H et al. A step-up approach or open necrosectomy for necrotizing pancreatits. NEJM 2010, n=88

Management of infection in severe acute pancreatitis: conclusions

1) Prevention:
   - monitor for IAH
   - start enteral jejunal feeding < 48 h

2) Diagnosis:
   - culture at least 2x/week and more in case of deterioration
   - use FNA (+PCT?)

3) Treatment:
   - no prophylaxis
   - if empirical therapy is started: preference for carbapenems
   - recommend ERCP judiciously
   - “there is nothing that cold steel can not heal”: step up-approach