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EDITORIAL

Severe acute pancreatitis: Clinical course and management

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Abstract

Severe acute pancreatitis (SAP) develops in about 25% of patients with acute pancreatitis (AP). Severity of AP is linked to the presence of systemic organ dysfunctions and/or necrotizing pancreatitis pathomorphologically. Risk factors determining independently the outcome of SAP are early multi-organ failure, infection of necrosis and extended necrosis (> 50%). Up to one third of patients with necrotizing pancreatitis develop in the late course infection of necroses. Morbidity of SAP is biphasic, in the first week strongly related to early and persistence of organ or multi-organ dysfunction. Clinical sepsis caused by infected necrosis leading to multi-organ failure syndrome (MOFS) occurs in the later course after the first week. To predict sepsis, MOFS or deaths in the first 48-72 h, the highest predictive accuracy has been objectified for procalcitonin and IL-8; the Sepsis-Related Organ Failure Assessment (SOFA)-score predicts the outcome in the first 48 h, and provides a daily assessment of treatment response with a high positive predictive value. Contrast-enhanced CT provides the highest diagnostic accuracy for necrotizing pancreatitis when performed after the first week of disease. Patients who suffer early organ dysfunctions or at risk of developing a severe disease require early intensive care treatment. Early vigorous intravenous fluid replacement is of foremost importance. The goal is to decrease the hematocrit or restore normal cardiocirculatory functions. Antibiotic prophylaxis has not been shown as an effective preventive treatment. Early enteral feeding is based on a high level of evidence, resulting in a reduction of local and systemic infection. Patients suffering infected necrosis causing clinical sepsis, pancreatic abscess or surgical acute abdomen are candidates for early intervention. Hospital mortality of SAP after interventional or surgical debridement has decreased in high volume centers to below 20%.

INTRODUCTION

Dealing with the clinical course of acute pancreatitis (AP) and the management of severe acute pancreatitis (SAP) are complicated by limited understanding of pathogenesis and multi-causality of the disease, uncertainties to predict outcome and a few effective treatment modalities. AP comprises clinically a mild oedematous-interstitial inflammation, which is a self-limiting disease, and a severe type of AP with a local necrotizing inflammation and systemic complications. Despite the importance of recognizing severe disease early in the course, many patients initially identified as having mild disease, progress to severe pancreatitis over the initial period of disease. Clinical studies and experimental new data have led to considerable progress in understanding the pathophysiological events of the early period of human AP, but the underlying processes leading to acinus cell necroses and the propagation of the necrotizing inflammation by impaired microcirculation of pancreatic tissue compartments in the initial 48-72 h, are still unknown to a large extent. Hence, management of human AP has been empiric and conflicting opinions are still present regarding medical and surgical management concepts.

PATTERN OF INFLAMMATION

The tissue response of the pancreas to an injury like acinus cell necrosis leads to production and liberation of proinflammatory cytokines, chemokines and other biological active compounds[1-4]. Clinical and experimental studies have verified activation of local macrophages and attraction of activated polymorphonuclear cells (PMNs) as first-line players in the defense and limitation of pancreatic tissue injury[5-7]. Inflammatory mediators are primarily released from the splanchnic area and gain access to the systemic compartment mainly by lymphatic, portal vein and suprahepatic circulation[1,8]. The lungs are the first

Table 1 Severe acute pancreatitis: Gut barrier dysfunction causes local changes and systemic complications

Local	Systemic consequences
Mucosal ischemia[10,15,16]	Priming of neutrophils[20-22]
Disruption of mucosal epithelial integrity[17]	Endotoxemia[14,23,24]
Reperfusion injury of mucosal epithelia[18]	Bacterial translocation[25-27]
Increase of intestinal permeability[19]	Cytokine overproduction[1,2,28]
Gram-negative intestinal bacterial overgrowth[11]	Impaired systemic immunity[29,30]
Impaired mucosal immunity[11]	

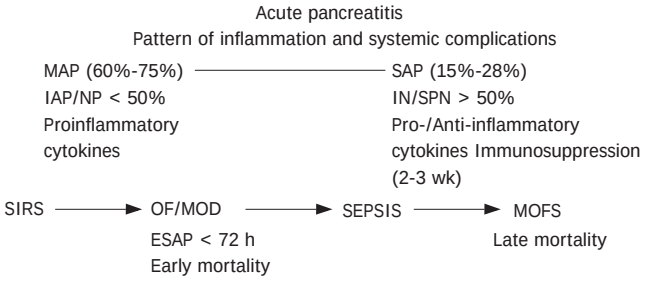

Figure 1 Pattern of inflammation and systemic complications in acute pancreatitis. MAP: Mild acute pancreatitis; SAP: Severe acute pancreatitis; IAP: Intestinal oedematous pancreatitis; NP: Necrotizing pancreatitis; IN: Infected necrosis; SPN: sterile pancreatic necrosis; SIRS: severe inflammatory response syndrome; OF: Organ failure; MOD: Multiorgan failure; SEPSIS: Leukocytes > 10 000/mm^3 + fever > 38.5 rectal/> 48 h + metabolic acidosis base excess > -4 mmol/L; MOFS: Multiorgan failure syndrome; ESAP: Early severe acute pancreatitis.

pass taker of the porto-hepatic blood and lymph of the splanchnic compartments enriched of activated PMNs, cytokines and other biological active compounds. Gut barrier failure, with the ensuing translocation of bacteria and endotoxin, has been proposed as a major contributor to the development of local infection and multi-organ failure in SAP[9]. Evidence of the association between gut injury and the subsequent development of infected necroses and distant organ failure continues to increase. Intestinal permeability disturbances have been found in humans with SAP 72 h after onset, correlating strongly with clinical outcome[10]: the increase of permeability was significantly higher in patients who developed multi-organ failure and/or died compared to patients suffering from mild attacks[11]. Intestinal permeability increases gradually during the course of SAP reaching a maximum at the end of the first week[12]. In a recent prospective study of patients with AP, endotoxemia as a consequence of increase of gut permeability was found on the day of admission to the hospital significantly more common and of greater magnitude in severe attacks than in those with mild attacks, in non-survivors than in survivors, and in patients who developed multi-organ failure than in those who did not[13,14] (Table 1).

The peritoneal compartment is the site of pro-inflammatory reaction to pancreatic necrosis, whereas an anti-inflammatory response dominates in the lymph collected from the thoracic duct, as well as in the systemic circulation during the first week after onset of systemic complications[1]. The cytokine levels in the blood and lymph are closely associated with the severity of illness on admission, the magnitude of multi-organ failure syndrome (MOFS) and the outcome as well[1,2]. Correlated with local and systemic complications, a compartmentalization of the inflammatory responses has been objectified. Local inflammatory cytokines at high concentrations are found in the portal and splanchnic circulation at the same time when in the systemic blood compartment anti-inflammatory compounds prevail over inflammatory cytokines. In SAP, a compensatory anti-inflammatory response affects the immunocompetence[30,31]. Patients with SAP show impaired immune response in regard to reduced HLA-DR expression of monocytes and macrophages[29,32], reduced numbers of CD4- and CD8-positive T-cells[33,34], an impairment of mononuclear phagocytic capacity[35] and an increase of the anti-inflammatory cytokine IL-10 and IL-1 receptor antagonist[36]. Reduced immune competence, as objectified by reduced expression of HLA-DR of monocytes and macrophages, predicts the development of organ failure and is associated with secondary infection[29] (Figure 1).

CLASSIFICATION OF ACUTE PANCREATITIS

At the beginning of the 1980s, the morphologic feature of SAP was established by the definition of infected and sterile necrosis, pancreatic abscess and postacute pseudocysts as the principal morphologic and bacteriologic criteria for clinical severity and considered to be determinants of the clinical course[37]. Macroscopically, necrotizing pancreatitis is characterized by focal or diffuse areas of devitalized parenchyma frequently associated with peripancreatic fatty tissue necroses extending sometimes to retroperitoneal spaces up to the pelvis. Intrapancreatic hemorrhage is variably present and may lead to an acute abdominal compartment syndrome. Infection of necrosis occurs in up to 30% of all patients with necrotizing pancreatitis[27,38]. In the clinical setting of AP, post-acute pseudocysts and pancreatic abscess are late consequences of the disease[39]. In both subgroups of AP, an inflammatory wall is developed which separates the inflammatory processes from the surrounding tissues. Both features have differences in clinical symptomatology and associated morbidity. Peripancreatic fluid collection that arises early during the course of AP is frequently a sign of severity. However, in most instances peripancreatic fluid collection disappears without any treatment[40].

The Atlanta Classification is accepted worldwide as the first clinical reliable classification system of AP. But the accumulation of clinical data forces a revision of the Atlanta criteria of severity. Organ failure has been recognized as a more important determinant of survival than the extent of pancreatic necroses. Particularly early multi-organ failure at admission or in the first days predicts strongly the clinical course and the outcome. Severity of organ failure using multi-step criteria as introduced for septic patients by the SOFA-score is considered clinically relevant and increasingly applied for severity scoring and predicting outcome[41]. The SOFA criteria for systemic

Table 2 Clinical course of AP/SAP

	Clinical	Pathophysiologic process
Early: d 1-10 after HA ESAP in about 20% of SAP	Hypovolemia Abdominal pain Dysfunction Pulmonary Renal Cardiocirculatory Liver Intestine	Fluid sequestration Liberation of pro- and anti-inflammatory cytokines Endotoxemia Liberation of vasoactive substances Disturbance of blood coagulation Translocation of endotoxin and bacteria
Late > 2 wk after HA	Local and systemic septic complications IN, SPN	Bacterial translocation CARS Anti-inflammatory reaction Immunosuppression

AP: Acute pancreatitis; SAP: Severe acute pancreatitis; ESAP: Early severe acute pancreatitis; HA: Hospital admission; IN: Infected necrosis; SPN: Sterile pancreatic necrosis; CARS: Compensatory antiinflammatory syndrome.

organ dysfunctions are clinically more reliable for decision making than the Atlanta criteria.

CLINICAL COURSE OF SAP

Acute pancreatitis is not a stable disease. Increasing amounts of intrapancreatic and retroperitoneal necroses are closely related to the frequency and severity of local and systemic complications[27]. About 70%-80% of AP takes a mild course and is associated only with minimal organ dysfunctions. First clinical signs are abdominal pain located in the epigastrium, frequently radiating into the midback (Table 2). Clinical improvement can easily be achieved by fluid replacement, a pain treatment and re-institution of regular food intake. The initial 2-4 d after onset of symptoms are most important, when about 15%-25% of patients with AP take the course of a severe disease. Based on clinical and experimental data, this period is characterized by an initial hypovolaemic state[42-44]. In SAP, hypotension or even shock occurs as a consequence of sequestration of protein-rich fluids into the pancreas, the retroperitoneal spaces and the abdominal cavity. The initial systemic inflammatory response syndrome causes a hyperinflammatory reaction exerting systemic organ dysfunctions of the lungs, kidneys, cardiocirculatory system and splanchnic intestinal compartments[45,46]. Acute fluid collections arise early in the course of severe acute pancreatitis, lack a well-defined wall and are usually peripancreatic in location, and usually resolve without sequelae but may evolve into pancreatic pseudocysts or abscesses. Acute fluid collections rarely require drainage. About 60%-70% of fluid collection resolves spontaneously and has no connection with the pancreatic duct system[47].

EARLY SEVERE ACUTE PANCREATITIS

About 20% of patients with SAP develop in the 72 h after onset of the disease organ failure or even have organ- or multi-organ failure at admission to hospitals[48]. Despite application of maximum intensive care treatment, 30%-50% of the patients with early severe acute pancreatitis do not promptly respond to ICU treatment and take a complicated course with persistence of multi-system organ dysfunctions. Patients suffering from early and persistent multi-organ insufficiency syndrome have a high risk of mortality[49]. Recently it has been shown that severe organ failure within the first week after onset of AP before any kind of intervention is closely linked to clinically relevant pancreatic infection which occurs two weeks later[50]. Early multi-organ dysfunction syndrome (MODS) obviously triggers additional mechanisms that render bacterial translocation into clinically manifested sepsis. Early onset MODS > 2 organs has proved to be the predominant risk factor for death. Early mortality in the first 6-10 d of SAP is caused by severe inflammatory response syndrome (SIRS) associated with early multi-organ insufficiency syndrome (Table 3). Early mortality was reported between 42% and 60%[51-53].

Table 3 Severe acute pancreatitis-early organ failure

Admission			Dynamic of organ failure	Hospital mortality
ESAP (n = 47)	SOF	25 (53%)	Reversible 9 develop MOF 14 (30%)	42%
	MOF	22 (47%)	Reversible 1 progress to MOFS 21 (95%)	
SAP (n = 111)	OF (-)	30 (27%)		
	SOF	26 (23%)		14%
	MOF	55 (50%)		

ESAP: Early severe acute pancreatitis; SOF: Single organ failure; MOF: Multiorgan failure; SAP: Severe acute pancreatitis; OF: Organ failure. Reversibility or assistance in spite of maximum intensive care treatment of early organ failure or early organ failure syndrome (n = 158)[48].

Presence of necrosis and infection

Gross destruction of the pancreatic gland by tissue necroses is observed in about 20% of patients with AP and takes place in the first week after onset[54]. Experimental and clinical observations reveal that development of pancreatic necrosis is accompanied by an increase of local and systemic organ complications, increasing the risk of morbidity and mortality compared to patients with interstitial-oedematous pancreatitis[55,56] (Figure 2). Most patients who develop early or late organ failure suffer from necrotizing pancreatitis. Autopsy data and surgical results have verified that more than 80% of deaths are correlated with the presence of necroses. The highest risk for local and systemic complications is seen in patients who show extended necrosis of more than ⩾ 50% of the pancreas by magnetic resonance tomography (MRT) or contrast-enhanced computer tomography (CECT)[57,58]. Patients with sterile extended pancreatic necroses (> 50%) display clinically signs of sepsis including organ dysfunctions, septic fever, leucocytosis, hyperdynamic cardiocirculatory state and intestinal motility disorder. To discriminate clinical infection from sterile necrosis, the use of sepsis criteria is not reliable in patients with extended sterile necrosis.

In addition to the presence of pancreatic parenchymal necrosis, the occurrence and extent of the necrotizing process into extrapancreatic retroperitoneal fatty tissue

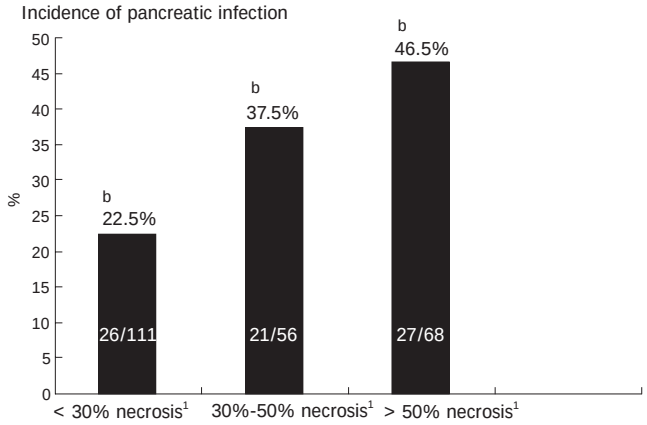

Figure 2 Relation between bacterial infection and extent of necrosis in 225 patients with severe acute pancreatitis. [1]On the basis of contrast-enhanced CT. [b]P = 0.008 between the groups, Cochran-Armitage trend test.

spaces including tissue compartments of the mesentery of the small and large bowel, the peri-renal fat and the para- and retrocolic compartments, are important factors influencing the course of the disease and strongly affect the clinical severity[59]. The overall infection rate of pancreatic tissue in necrotizing pancreatitis is up to 30% and may increase to 70% in the 3rd wk[27] (Table 4).

The setting of pancreatic infection includes infected necrosis, pancreatic abscess and infected pancreatic pseudocysts. The bacteriological analysis of puncture aspirates or of intraoperative smears reveals predominantly gram-negative microbes deriving from the intestine. *Escherichia coli* was the most frequent pathogen followed by *Enterococcus* and *Klebsiella*[27]. However, in recent years a shift of the bacterial pattern has been observed towards more gram-positive bacteria like *Staph aureus* and *Enterobacteriaceae*[60,61]. The presence of candida species in infected necroses has been observed in 5%-15%[62]. Candida patients have a higher mortality and experience more systemic complications than patients without candida infections of necroses. Recent data about the routine use of prophylactic antibiotics provided evidence that application of antibiotics contributes to the development of candida infection and to changes in bacterial spectrum of infected necroses with an increased incidence of gram-positive infections[62,63].

CT-guided fine needle aspiration (FNA) of the necrotic area is a safe procedure to diagnose infection, identify bacteria and institute appropriate therapy. To distinguish pancreatic inflammation from secondary infection, gram staining and culture must be performed after guided aspiration[64]. The knowledge of the bacteria and candida species and the pattern of chemo-resistance may lead to a rational antibiotic treatment.

MANAGEMENT OF SAP: PREDICTION OF SEVERITY AND OUTCOME

The management of patients with AP is challenging due to late hospitalization after onset of the acute attack and difficulty in distinguishing mild from severe disease in the first 48-72 h. Identification of risk factors for the development of necrotizing pancreatitis within the initial 24 h of hospitalization is of potential clinical importance. Patients who display at admission organ dysfunctions or an Apache Ⅱ score ⩾ 8[65] or C-reactive protein (CRP) > 120 mg/dL[66] or procalcitonin > 1.8 ng/mL[67] or a hematocrit > 44[68] should have early intensive care for optimal surveillance and ICU treatment. The use of early CECT or MRI for determination of severity is limited by several factors: (a) only a quarter of patients with acute pancreatitis develop necroses; (b) pancreatic necroses may not develop in the first 48 h; and (c) the presence of pancreatic necroses and the amount of necroses does not strongly correlate with the development of organ failure (Figure 3)[69]. The CECT based Balthazar classification shows the highest diagnostic and predictive accuracy when performed after the first week of disease. The APACHE Ⅱ scoring and the sequential Sepsis-Related Organ Failure Assessment (SOFA) have a highly reliable sensitivity and specificity and positive predictive value for the degree of severity of SAP. APACHE Ⅱ-, Marshall- and SOFA score can objectify the responses of the patients to intensive care measures (Table 5) on a daily basis. The biochemical parameters, CRP, procalcitonin and IL-8 have a high predictive accuracy for the degree of severity of necrotising pancreatitis in the first days. Procalcitonin > 1.4 ng/mL has a diagnostic accuracy of 70% for infection of necrosis; and procalcitonin of > 3.8 ng/mL predicts MODS with a diagnostic accuracy of 92%[72] (Table 6).

Table 4 Frequency of pancreatic infection in 427 patients[1] with necrotizing pancreatitis[2]

		NP (%)	AP (%)
Infected necrosis	99	23.2	6.9
Pancreatic abscess	40	9.4	2.8
Infected pseudocyst after AP	7	1.6	0.5
Total	146	34.2	10.1

[1]Pancreatic necrosis/extrapancreatic fatty tissue necrosis, pancreatic abscess, postacute pseudocyst. [2]5/1982-12/1996 Department of General Surgery, University of Ulm.

First line treatment of SAP

Admission hematocrit of > 47 and a failure of admission hematocrit to decrease at 24 h has been identified as reliable criteria of hemoconcentration of SAP in the very early period of the disease[42-44]. Vigorous intravenous fluid resuscitation is required to overcome systemic hypovolemia caused by intravascular fluid loss[73,74]. Intravenous fluid substitution for patients with predicted SAP should be established with 250-350 mL/h for the first 48 h[42]. Restoration of normal cardiocirculatory functions objectified by heart-rate, systolic or mean arterial blood pressure, an oxygen saturation of venous blood of > 95%, absence of a base deficit > 5 μmol/L and urine flow of ⩾ 50 mL/h are decisive criteria of treatment response.

In mild biliary acute pancreatitis, endoscopic retrograde cholangiopancreatography (ERCP) and removal of common bile duct stones do not change the natural course

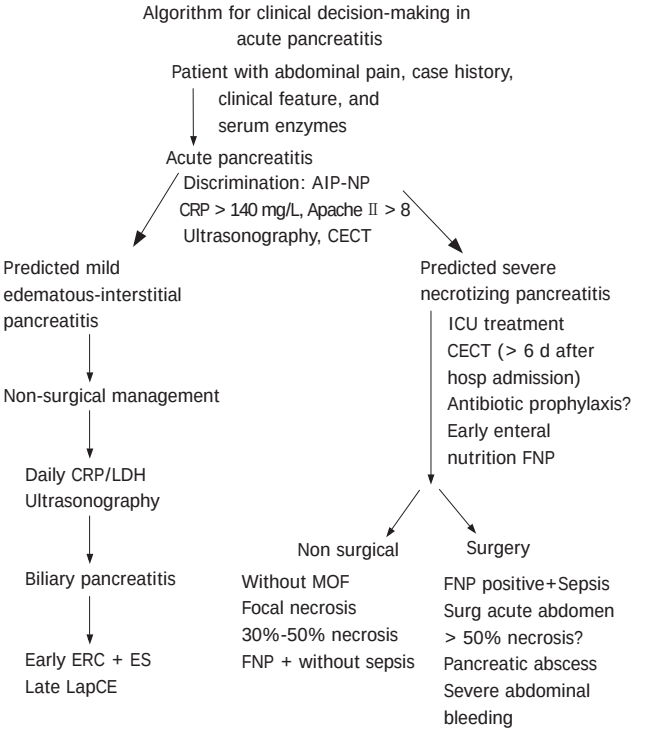

Figure 3 Algorithm for clinical decision making in acute pancreatitis. AIP: Acute interstitial pancreatitis; NP: Necrotizing pancreatitis; CRP: C reactive protein; CECT: Contrast-enhanced computer tomography; LDH: Lactate dehydrogenase; ERC: Endoscopic retrograde cholangiography; ES: Endoscopic sphincterotomy; CE: Laparoscopic cholecystectomy; FNP: Fine needle procedure; MOF: Multiorgan failure syndrome.

Table 5 Severe acute pancreatitis: Clinical systems to predict prognosis

	Cut-off	Time	Reference
Ranson	> 2 points	> 48 h	SGO 1974[71]
Apache Ⅱ	> 9 points	daily	Br J Surg 1990[65]
Balthazar	C, D, E	> first week	Radiology 1990[69]
Marshall score	> 3 points	72 h	Crit Car Med 1995[45]
MOF/Goris	> 1 point	48 h	Arch Surg 1985[46]
SOFA	> 4 points	48 h/d	Crit Car Med 1996[41]

MOF: Multiorgan failure; SOFA: Sepsis-related organ failure assessment.

of pancreatitis. ERCP, endoscopic sphincterotomy and stone removal are applied after subsidence of clinical signs of AP. In severe biliary pancreatitis, early sphincterotomy and stone extraction are beneficial when common bile duct stone has been diagnosed to be associated with SAP. Early endoscopic extraction of common bile duct stones brings about disappearance of cholestasis and decompression of the pancreatic main duct. A significant reduction of biliary and systemic morbidity has been objectified by two randomized controlled trials (RCTs)[75-77]. However, ERCP and sphincterotomy in SAP increases the risk of an additional pancreatitic trauma in up to 10% of patients and may increase the risk of additional cholangitis episodes during the course of SAP.

Antibiotic prophylaxis turned out to be not very effective in regard to avoidance or reduction of infection of necrosis and associated systemic complications[78]. Two randomized

Table 6 Early prediction of infected necrosis, infected necrosis + MODS and death using biochemical parameters

	Cut-off	Sensitivity (%)	Specificity (%)	Accuracy (%)
Prediction of infected necrosis				
PCT	⩾ 1.4 ng/mL	75	68	69[a]
CRP	⩾ 400 mg/L	29	92	76
Prediction of infected necrosis and MODS				
PCT	⩾ 3.8 ng/mL	80	93	92[a]
CRP	⩾ 410 mg/L	35	93	87
Prediction of death				
PCT	⩾ 3.8 ng/mL	82	88	88[a]
Prediction of IN and MODS or death				
PCT	⩾ 3.8 ng/mL	76	94	92[a]
CRP	⩾ 400 mg/L	35	92	84

PCT: Randomized controlled trial; CRP: C reactive protein; MODS: Multiorgan dysfunction syndrome; IN: Infected necrosis. Receiver operating curve-analysis based on d 3 and 4 onset of symptoms, [a]P < 0.05-0.004, Rau, Annals of Surgery 2007[72].

Table 7 Severe acute pancreatitis-antibiotic prophylaxis is inefficient in severe acute pancreatitis; results of two randomized controlled double-blind multicentric trials

	Isenmann[79]		Dellinger[80]	
	2004	*P* value	2005	*P* value
Patients (*n*)	114		100	
Treatment (*n*)[1]	48		40	
Placebo (*n*)	41		40	
Infection of necrosis				
Treatment	12%[1]	NS	23%[2]	NS
Placebo	14%[1]		15%[2]	
Need for surgery				
Treatment	17%[1]	NS	23%[2]	NS
Placebo	11%[1]		24%[2]	
Hospital mortality				
Treatment	12%[1]	NS	20%[2]	NS
Placebo	9%[1]		18%[2]	

[1]Statistical comparison of treatment and placebo group data 2004; [2]Data 2005.

double blinded prospective controlled multi-center trials proved antibiotic prophylaxis ineffective in regard to reduction of infection of necrosis and hospital mortality[79,80] (Table 7). But patients with pulmonary infection and who show a positive blood culture associated with signs of sepsis should be treated with antibiotics. Enteral feeding (EN) in SAP reduces significantly the infection rate of necrosis and lowers the need for surgical interventions[81-85]. However, hospital mortality and non-infectious complications are not altered by enteral feeding compared to parenteral nutrition (Table 8). The beneficial effect of EN may be more pronounced if it is instituted early[86].

Non-surgical ICU-management is successful in most patients with AP who have sterile pancreatic necroses and who do not develop organ failure (Table 9). Patients having pancreatic necroses and who are fine needle procedure (FNP)-positive but do not show clinical signs of sepsis, do not need surgical intervention[87-89].

Interventional treatment of infected necrosis

Surgical debridement has been documented to be

Table 8 Severe acute pancreatitis-enteral feeding reduces infection in the need for surgical intervention

Benefits of enteral nutrition	Lower infections ($P = 0.004$)
	Reduced surgical interventions ($P = 0.05$)
	Reduced LHS-2.9 d ($P < 0.001$)
Differences	Hospital mortality ($P = 0.3$)
	Non-infectious complications ($P = 0.16$)

LHS: Length of hospital stay. Enteral feeding *vs* parenteral nutrition, results of 6 RCTs, meta-analysis of 263 patients[81-86].

Table 9 Severe acute pancreatitis-surgical and non-surgical treatment: Ulm Experience: 1568 patients[1] *n* (%)

	Patients	Conservative	Surgery/Intervention
Interstitial-oedematous	1071 (68.3)	1056 (98.6)	15 (1.4)[2]
Necrotizing pancreatitis	359 (22.9)	95 (26.5)	264 (73.5)
Sterile necrosis	227	85 (37.5)	142 (62.5)
Infected necrosis	132	10 (7.6)	122 (92.4)
Pancreatic abscess	42 (2.7)	3 (7.1)	39 (92.9)
Postacute pseudocyst	96 (6.1)	22 (22.9)	74 (77.1)

[1]5/1982-12/1999 Department of General Surgery, University of Ulm, Germany. [2]Biliary tract surgery not included.

effective for patients with proven infected necrosis and progressive clinical sepsis. Patients with SAP who develop a surgical acute abdomen during the course of ICU treatment need emergency surgery to avoid development of abdominal compartment syndrome[57] or consequences of intestinal perforations. Patients with extended sterile necrosis (> 50% of the pancreas) are at high risk for infected necrosis with the consequence of progressive MODS. These patients are candidates for surgical and interventional measures after their clinical signs show non-response to maximum intensive care treatment. Patients with infected necrosis are managed by surgical and interventional treatment modalities (Table 10).

A variety of surgical treatment modalities are currently in use. The advantages of minimally invasive interventional debridement, whether performed by laparoscopic techniques or by a retroperitoneal approach, are up to now not based on results of controlled clinical trials. By use of minimal invasive techniques for infected necrosis in the late course of disease, the morbidity remains high for several days. Two to 7 reoperations with lavage are necessary to interrupt systemic complications of the local inflammatory process[96-103] (Table 11). An open surgical debridement combined with continuous short-term lavage of the lesser sack interrupts clinical sepsis in patients suffering from extended necrosis with infection accompanied by multi-system organ failure. The early treatment related morbidity is much lower in patients treated with open surgery than after first pass of minimal invasive debridement. The frequency of reoperation is between 25% and 40% and up to 100% in patients after minimal access intervention. Hospital mortality in high volume centers is below 20% after open necrosectomy plus bursa lavage and after minimal invasive surgical approach as well.

Table 10 Results of open surgical debridement of necrotizing pancreatitis using surgical debridement and local bursa lavage

	Complication			Hospital mortality
	n	Postop, *n* (%)	Reop, *n* (%)	*n* (%)
Pederzoli 1990[90]	191	55 (29)	34 (18)	40 (21)
Beger 1999[92]	221	122 (55)	93 (42)	46 (21)
Mai 2000[61]	27	10 (37)	6 (22)	5 (18)
Hungness 2002[93]	26		4 (15.4)	6 (23)
Farkas 2006[94]	220	43%	48 (22)	17 (7.7)
Howard 2007[95]	102	83 (81)	69 (68)	12 (11.8)
1990-2007	787	43%	29.60%	14.70%

Table 11 Results of minimal invasive interventional treatment of necrotizing pancreatitis: Minimal invasive debridement + local lavage

	n	Infect. necrosis (%)	Apache II	Time O-S	Early morbidity (%)	OP/ pts	Hospital mortality (%)
Freeny 1998[96]	34	100	-				20
Goiuzi 1999[97]	32	81	26				15
Carter 2000[98]	10	90		24 d	10	3	20
Horvath 2001[99]	6	100			33		0
Castellanos 2002[100]	15	100			40		27
Connor 2003[101]	24	58	8		88	4	25
Zhou 2003[102]	12	58		72/102			0
Connor 2005[103]	47	81	9	28 d	92	3	19
1998-2006	156 pts	83			70.6		18.3

OP: Operation per patient; O: Onset of disease; S: Surgery.

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