Pancreatology 15 (2015) 360–365

Contents lists available at ScienceDirect

Pancreatology

journal homepage: www.elsevier.com/locate/pan

Original article

Late infection of pancreatic necrosis: A separate entity in necrotizing pancreatitis with low mortality

Qiang Guo [a], Ang Li [a], Qing Xia [b], Weiming Hu [a, *]

[a] Pancreatic Surgery, West China Hospital, Sichuan University, Chengdu, 610041 Sichuan Province, China
[b] Department of Integrated Traditional Chinese and Western Medicine, West China Hospital, Sichuan University, Chengdu, 610041 Sichuan Province, China

ARTICLE INFO

Article history:
Available online 21 May 2015

Keywords:
Acute pancreatitis
Duration
Infection
Intervention
Mortality
Organ failure

ABSTRACT

Background: Several studies have examined on the timing of the onset of infected necrosis and organ failure. The duration of these two complications and the effects of different durations of these two complications have not been mentioned. Our aim was to investigate the durations of these two complications and the corresponding effects of the different durations.
Methods: A post-hoc analysis was performed on a prospective database containing 578 patients with necrotizing pancreatitis. The patients who received intervention were divided into subgroups based on different durations of the two complications, and the outcomes were compared.
Results: The mortality rate in patients with late infection (occurred after 30 days) was lower than in the early (infection occurred within 30 days) group (3% vs. 22%, $P < 0.05$). The mortality rate in patients with long duration (>7 days) of infection before intervention was similar with those patients with short duration (≤7 days) of infection (6/27 vs. 11/74; $P = 0.38$). The mortality rate in patients with long duration (>7 days) of organ failure before intervention was higher than in patients with short duration (≤7 days) of organ failure (31/99 vs. 18/184; $P < 0.001$).
Conclusion: Patients with late developed infection of pancreatic necrosis showed significantly better prognosis than patients with early infection. The duration of organ failure before intervention was correlated with mortality of necrotizing pancreatitis.

Acute pancreatitis (AP) is a common gastrointestinal disease, and its severity varies from mild to fulminant with high morbidity and mortality [1,2]. Treating AP is costly, especially in severe cases with long intensive care unit (ICU) stay [1]. Many studies attempt to reduce mortality by preventing organ failure and infection, which are considered to be the two major causes of death in patients with necrotizing pancreatitis [3–5]. Several studies focus on the timing of the onset of infected necrosis and organ failure [6–9]. However, the duration of these two complications and the corresponding effects of the different durations have not been investigated.

Infected necrosis can be diagnosed based on imaging signs of gas bubbles in peripancreatic collections on computed tomography (CT) or positive microbiological culture obtained by fine-needle aspiration (FNA) or intervention [10]. A study reported the timing of the onset of infected necrosis diagnosed by FNA and suggested that infected necrosis occurs at a median of 13 days after the onset of symptom and ranges from 3 days to 44 days [9]. Infection of necrosis can occur at any time after the onset of symptoms [6]. Many studies have documented that early development of organ failure (OF) is associated with higher mortality rate compared with late OF because late developed OF is less severe than early developed OF [11,12]. Thus, a rate difference in complications and mortality might exist between the patients with early and late infection of necrosis. Many studies indicate that organ failure, particularly persistent organ failure, is significantly associated with mortality [13,14]. However, information on the duration of organ failure is not found in most of these studies.

This study investigated the timing of the onset of infected necrosis and organ failure in patients with necrotizing pancreatitis. Patients who received intervention were divided into subgroups based on different durations of these two complications, and the outcomes of the subgroups were compared. The primary aim of this study was to determine whether there is a difference in outcomes between the patients with early and late infection of necrosis. The

* Corresponding author.
E-mail address: huweiming64@gmail.com (W. Hu).

http://dx.doi.org/10.1016/j.pan.2015.05.459

secondary aim was to verify whether the outcomes differ between the different durations of the two complications.

Methods

Patients

Patients diagnosed with pancreatic necrosis or peripancreatic necrosis confirmed by contrast-enhanced computed tomography (CECT) were included in a prospective cohort study from January 2009 to March 2013 in West China Hospital. During the study period, all patients admitted with necrotizing pancreatitis were registered in a prospective database. We performed a post-hoc analysis in the prospective database of 578 patients with necrotizing pancreatitis.

Treatment protocol

After admission, all components of the modified Marshall scoring system were recorded every day during the first week of onset. All components of the Acute Physiology and Chronic Health Examination (APACHE) II scoring system were recorded upon admission. Body temperature was measured at least three times daily; when the temperature was higher than 38.0 °C, a blood culture was obtained. Routine FNA was not performed on patients with pancreatic necrosis. All patients initially received non-interventional treatment [15]. After admission, antibiotics were administered to patients for not more than 7 days, unless they had persistent clinical manifestations of sepsis. During this treatment, CECT was performed 7 days−10 days after onset, and the CT severity index was recorded. Unenhanced CT was performed repeatedly if necessary. When abdominal pain, severe clinical deterioration, or development of clinical signs of sepsis persisted or recurred, a second CECT was conducted. The CT severity index was also recorded. Patients with suspected or confirmed infected necrosis were advised to undergo surgical treatment. In this study, intervention was postponed until approximately 4 weeks after the onset of disease, whenever possible. However, when severe clinical deterioration persisted, a prompt intervention was carried out. Open pancreatic necrosectomy, retroperitoneal pancreatic necrosectomy, or primary percutaneous catheter drainage with pigtail plastic stents were the possible types of intervention. Cultures were obtained during all primary procedures to confirm the diagnosis of infected necrosis. All components of the modified Marshall scoring system were also collected at the time of intervention. This study was conducted in accordance with the principles in the Declaration of Helsinki. All patients or their legal representatives provided written informed consent. The ethics review board of West China Hospital approved the study.

Definitions and groups

Infected necrosis was defined as a positive culture of pancreatic necrosis or peripancreatic necrosis obtained through FNA or from the first operation or the presence of gas in the peripancreatic collection on CECT. Suspected infected necrosis was defined as persistent clinical manifestations of sepsis without the presence of gas in the peripancreatic collection on CECT. Based on the timing of the onset of infected necrosis, all included patients with documented infected necrosis were divided into two groups, namely, the early and late infected groups. Early infected necrosis was defined as severe clinical deterioration or development of clinical signs of sepsis with or without gas in peripancreatic collections on CT that occurred within 1 month (≤30 days). Late infected necrosis was defined as the onset of severe clinical deterioration or development of clinical signs of sepsis that started 1 month after the onset of symptoms with first documented positive imaging signs occurred 1 month after onset (Fig. 1).

Data collection and statistical analysis

Characteristics and outcomes of the subdivided groups were compared. The following data were collected from the prospective database: patient demographics, American Society of Anesthesiologists classification, etiology, APACHE II score on admission, modified Marshall score, CT findings, laboratory findings, surgical type, duration of antibiotic usage, time from onset to intervention, presence of infectious complications and organ failure, clinical course, and mortality.

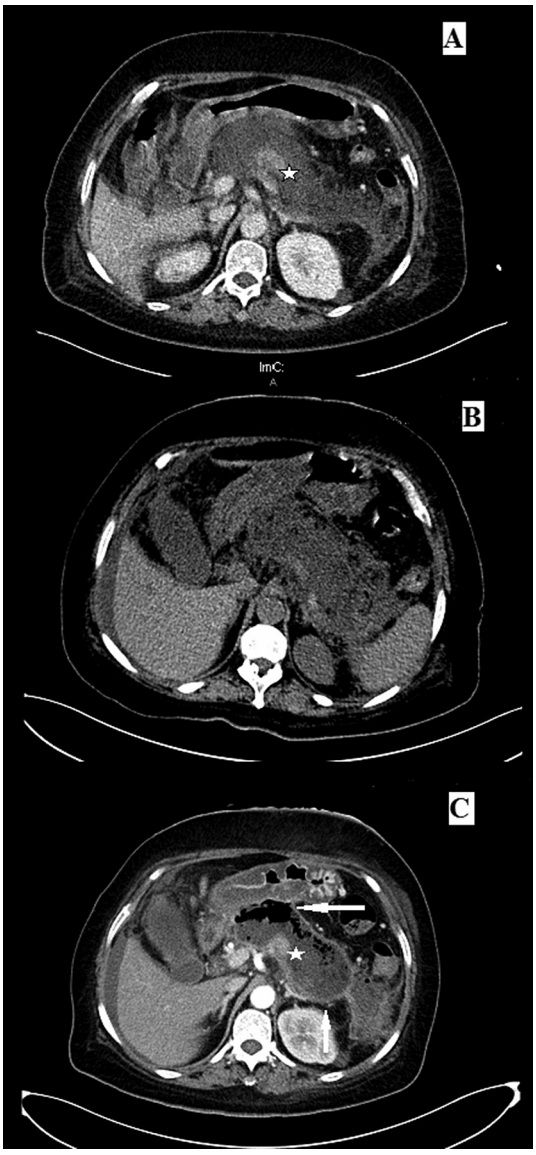

Fig. 1. (A) CECT scan of a 51 year-old female patient with acute pancreatitis 9 days after onset of symptoms. Normal enhancement of a part of the body of the pancreas (white asterisks) existed. (B) In unenhanced CT performed 23 days after onset, no gas bubbles were found. (C) About 32 days after onset, the patient started to have persistent fever, and a CECT scan was performed 3 days later. The scan revealed a walled-off necrotic collection complicated by infection (white asterisks denote normal enhancing pancreas; the white arrow above points at the gas bubbles in the necrotic collection, and the white arrow below points at the wall of the necrotic collection).

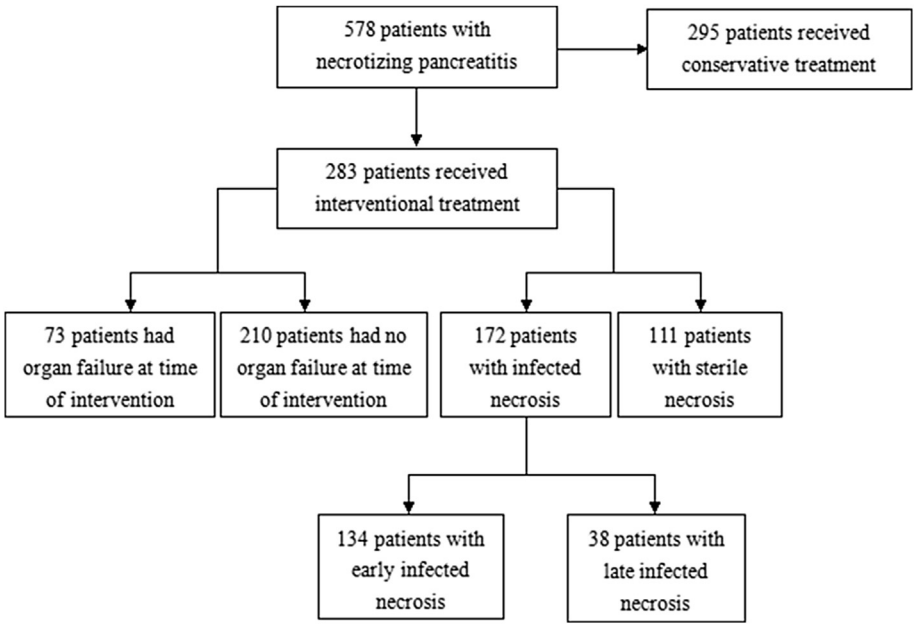

Fig. 2. Study population.

Continuous data are presented as median with interquartile range. The Mann–Whitney test was performed to determine differences. Proportions were compared by the chi-square, Fisher's exact, or linear-by-linear association test. A two-sided $P < 0.05$ was considered statistically significant. All statistical analyses were performed using SPSS for Windows version 16.0.2 (SPSS, Chicago, IL, USA).

Results

A total of 578 patients with pancreatic necrosis or only peripancreatic necrosis were included. Intervention was performed in 283 of the 578 patients (Fig. 2). Table 1 shows the data on the timing of the onset of infected necrosis and organ failure. Organ failure occurred at a median of 4 days after onset, and most occurred within 14 days (86%). Infected necrosis occurred at a median of 27 days after onset, and most occurred after 14 days (99%).

A total of 38 patients exhibited severe clinical deterioration or development of clinical signs of sepsis with first documented positive imaging signs that occurred 1 month after onset. These patients were included in the late group. The rest of the 134 patients were included in the early group. Characteristics and outcomes of the two groups are shown in Table 2. No differences were observed in age, sex, etiology, ASA classification, APACHE-II scores, CRP levels, surgical type, and duration of antibiotic usage. As shown in Table 2, the patients in the late infected necrosis group had lower modified Marshall score at the beginning of onset and before intervention than the patients with early infected necrosis. Time from onset to intervention in the late group was longer than in the early group (39 d vs. 30 d, $P < 0.001$). The mortality rate in the late group was also lower than in the early group (3% vs. 22%, $P = 0.003$; OR = 0.094; 95% confidence interval, 0.012–0.712).

Among the 283 patients who received intervention, 172 were confirmed to have infected necrosis by a positive culture. The mortality rates in patients with sterile and infected necroses were 15% (18/111) and 18% (31/172), respectively ($P = 0.52$). Gas bubbles on CT were found in 101 patients after a median of 24 days after onset. Ninety-nine of these patients were confirmed to have infected necrosis by a positive culture during the first intervention. The diagnostic accuracy reached 98%. The first intervention was performed during a median of 7 days after the positive imaging findings. The overall mortality rate with positive imaging findings was 18% (18/101), which is similar to patients without positive imaging findings (18/101 vs. 13/71, $P = 0.69$). The mortality rate in patients with long duration (intervention at 7 days later after CT was performed) of infection before intervention was similar with those patients with short duration (intervention within 7 days after CT was performed) of infection (6/27 vs. 11/74; $P = 0.38$). The mortality rate in patients with long duration (>7 days) of organ failure before intervention was higher than in patients with short duration (≤7 days) of organ failure (31/99 vs. 18/184; $P < 0.001$).

We divided the patients who received intervention into two groups, namely, survived and died groups. Patients who died had significantly higher preoperative modified Marshall score [median and IQR: 5 (3–7) vs. 1 (0–2); $P < 0.001$] and longer duration of

Table 1
Time of onset of complications.

Complications	Time of onset Median (range), days	≤14 days, No. (%)	>14 days, No. (%)
Organ failure	4 (1–50)	204 (86)	33 (14)
Pulmonary failure	3 (1–50)	179 (84)	34 (16)
Renal failure	5 (1–14)	110 (100)	0 (0)
Circulatory failure	4 (1–41)	51 (85)	9 (15)
Infected necrosis	27 (14–85)	1 (1)	171 (99)
Mortality	31 (7–79)	23 (31)	52 (69)

Table 2
Characteristics and outcomes of the patients who received interventional treatment with early or late infected necrosis.

Characteristic	Early infected necrosis ($N = 134$)	Late infected necrosis ($N = 38$)	P value
Age, median (IQR), y	46 (30–62)	48 (34–58)	0.25
Male, No. (%)	82 (61)	25 (66)	0.71
Etiology, No. (%)			
Biliary	64 (48)	16 (42)	0.58
Alcohol abuse	15 (11)	6 (16)	0.41
Others	55 (41)	16 (42)	0.99
BMI on admission, median (IQR)	30 (26–32)	27 (24–30)	0.15
APACHE II score on admission	8 (5–11)	8 (5–11)	0.56
Computed tomography			
CT severity index, median (IQR)	8 (6–10)	8 (6–10)	0.78
Pancreatic necrosis, No. (%)	91 (68)	29 (76)	0.37
Peripancreatic necrosis alone, No. (%)	33 (32)	6 (24)	0.37
Extent of pancreatic necrosis, No. (%)			0.51
<30%	53 (40)	16 (42)	
30%–50%	24 (23)	8 (29)	
>50%	38 (37)	9 (29)	
Organ failure			
Highest modified Marshall score in the first week of onset, median (IQR)	3 (2–4)	2 (1–3)	0.02
Persistent organ failure started in the first week of onset, No. (%)	53 (40)	9 (24)	0.09
Organ failure at time of intervention, No. (%)	35 (26)	4 (11)	0.049
Modified Marshall score at time of intervention, median (IQR)	2 (1–3)	1 (0–2)	0.001
Laboratory tests within 72 h of onset			
White blood cell count, median (IQR), 10^9/L	14.0 (11.8–17.9)	14.6 (12.0–18.4)	0.68
C-reactive protein, median (IQR), mg/L	192 (150–312)	204 (158–324)	0.46
Time (days) from onset to intervention, median (IQR)	30 (27–33)	39 (36–44)	<0.001
Surgical type			
Open pancreatic necrosectomy, No. (%)	84 (62)	21 (55)	0.45
Retroperitoneal pancreatic necrosectomy, No. (%)	25 (19)	11 (29)	0.18
Primary percutaneous catheter drainage, No. (%)	25 (19)	6 (16)	0.81
Duration (days) of antibiotic usage before intervention, median (IQR)	11 (7–14)	12 (7–16)	0.38
Mortality, No. (%)	30 (22)	1 (3)	0.003

BMI was calculated as weight in kilograms divided by height in meters squared.
APACHE, Acute Physiology and Chronic Health Examination; ASA, American Society of Anesthesiologists; BMI, body mass index; CT, computed tomography.

organ failure before intervention [median and IQR: 15 days (7 days–20 days) vs. 5 days (1 day–7 days); $P < 0.001$] than survivors (Table 3). Patients who died had similar duration of infected necrosis before intervention [median and IQR: 8 days (3 day–10 days) vs. 7 days (3 day–10 days); $P = 0.49$] with survivors.

Discussion

A large series of patients was used to evaluate the clinical outcome of different durations of infected necrosis and organ failure in this study. The results showed that patients with early infected necrosis had a worse prognosis than patients with late infected necrosis. In addition, mortality in patients with long duration of organ failure before intervention was significantly higher than in patients with short duration of organ failure before intervention. To the best of our knowledge, this study is the first to focus on the outcomes of these subgroups.

Infection of necrotizing pancreatitis is a well-accepted indication for interventional treatment; thus, elucidating the timing of infection is critical [15–17]. Several studies have assessed the time of onset of infected necrosis [6–9]. Some diagnoses were based on positive microbiological culture obtained at the first intervention [6,7], whereas others were based on FNA [8,9]. In a prospective study, 13 of 45 patients were diagnosed with infected necrosis within 14 days through open necrosectomy [7]. Another cohort study demonstrated that infected necrosis occurs at an average of 26 days after admission, and 18% (18/95) of the patients are diagnosed within 14 days [6]. The timing of the onset of infected necrosis diagnosed by FNA occurs at a median of 13 days after onset of symptoms and ranges from 3 days to 44 days [9]. In the present study, FNA was not performed preoperatively. Only one patient was diagnosed to have infected necrosis within 14 days. In the current series, even in the case of positive culture by FNA, intervention was usually postponed if clinically possible until the necrosis had become walled off, and results have shown improvement from this strategy [15–18]. Thus, the number of patients who received intervention within 14 days has been remarkably reduced in recent years. Two reports indicated that organ failure occurs 5 days after onset and 2 days after admission, which are similar with the results of the present study [7,8]. In the present study, 86% of the patients had organ failure within 14 days. These results indicate that the majority of infection of pancreatic necrosis started 14 days after onset, and the majority of organ failure occurred within 14 days.

We divided all the patients with documented infected necrosis into early and late infected groups based on the timing of the onset of infected necrosis. Compared with the patients with early

Table 3
Effects of organ failure and infected necrosis on mortality for patients who received intervention.

Characteristic	Survived	Died	P value
Organ failure at time of intervention, No./Total	41/73	32/73	<0.001
Infected necrosis, No./Total	141/172	31/172	0.75
Preoperative modified Marshall score, median, days	1	5	<0.001
Duration of organ failure before intervention, median, days	5	15	<0.001
Duration of infected necrosis, median, days	7	8	0.49

infected necrosis, patients in the late infected necrosis group had lower modified Marshall scores at the beginning of onset and before intervention. The mortality rate in the late group was also lower than in the early group (3% vs. 22%, $P < 0.05$). To our knowledge, this study is the first to evaluate the outcomes of different onset times of infected necrosis. The above mentioned results also support the earlier conclusion we made in our previous study that infection possessed a minor function in necrotizing pancreatitis [19]. First, from the pathophysiological aspect, SIRS is caused by the activation of an inflammatory cascade mediated by cytokines, such as tumor necrosis factor and interleukin-6 (IL-6), mononuclear cells, and the complement system. This inflammatory response involves the activation of macrophages, which are recruited into tissues and result in the development of MODS at an early stage [20]. As previously mentioned, organ failure is generally diagnosed earlier than infected necrosis. Organ failure at early stage is unrelated to infection [6]. At late stage, if infection could aggravate organ failure, the modified Marshall scores would be similar to those in the early group. However, based on our results, organ failure at this stage is likely unrelated to infection. Second, in this study, the time from onset to intervention in the late group was longer than in the early group (39 d vs. 30 d, $P < 0.001$). As we know, walled-off necrosis is a mature, encapsulated collection of pancreatic and/or peripancreatic necrosis with a well defined inflammatory wall; usually this maturation occurs $\geq$4 weeks after onset of necrotizing pancreatitis [10]. Intervention for infected walled-off necrosis is associated with a better outcome than those without walled-off necrosis [21]. The better outcome of late group might be the consequence of delayed intervention.

Detection of gas in peripancreatic collections by CECT always suggests a diagnosis of infection. The diagnostic sensitivity is remarkably high [8,22]. Other methods to diagnose or suspect infection were FNA and clinical signs. However, judgment of clinical deterioration is always objective and requires experience. FNA has a high accuracy but can carry a risk of related complications [23]. Furthermore, a prompt intervention is not suggested after a positive culture is obtained by FNA. Thus, therapeutic implications of FNA are limited. In the present study, gas bubbles on CT were found in 101 patients after a median of 24 days after onset. The diagnostic accuracy reached 98%. The mortality rate in patients who received intervention within 7 days after a positive CT was performed was comparable with that in patients who received intervention 7 days later (15% *vs.* 22%, $P = 0.38$). This result demonstrated that prompt intervention is unnecessary even with a convincing diagnosis after a 3 week time of onset. When we analyzed the effect of duration of infected necrosis on mortality, results suggested that patients who died had similar duration of infected necrosis before intervention [median and range: 8 days (0 day–15 days) vs. 7 days (0 day–14 days); $P = 0.49$] with survivors, which also support the aforementioned conclusion.

A previous study analyzed prognostic factors in patients undergoing surgery for severe necrotizing pancreatitis [24]. Results suggested that patients who died have higher preoperative Marshall and APACHE II scores than survivors, which were similar to the results obtained in this study. However, these studies did not assess organ failure at the time of intervention nor the relationship between different durations of organ failure and outcomes. The mortality rates were 44% in the patients with organ failure at time of intervention and 8% in the patients without organ failure ($P < 0.001$). The mortality rate in patients with long duration (>7 days) of organ failure before intervention was higher than in patients with short duration ($\leq$7 days) of organ failure (31/99 vs. 18/184; $P < 0.001$). When we analyzed the effects of organ failure on mortality, patients who died had significantly higher preoperative modified Marshall scores [median and IQR: 5 (3–7) vs. 1 (0–2); $P < 0.001$] and longer durations of organ failure before intervention [median and IQR: 15 days (7 days–20 days) vs. 5 days (1 day–7 days); $P < 0.001$] than survivors. To evaluate the outcome of necrotizing pancreatitis, future studies should focus on organ failure at the time of intervention and the duration of organ failure before intervention.

The limitations of this study are as follows. First, we did not perform FNA during the study period. The diagnosis of infected necrosis was based on CECT or the culture of necrotic collection obtained during intervention. Thus, the accurate timing of onset of infection is earlier than we described, and the accurate duration of infection is longer than we described. However, we could not perform CECT or FNA daily to determine the accurate timing of onset. We performed CECT or intervention based on suspicion of infection by close clinical observation. Second, we only evaluated mortality outcome. Other outcomes, such as the length of hospital stay or ICU stay, were not considered because we speculated that they cannot provide additional information for our objectives.

In conclusion, this study showed that the prognosis of patients with late infection of pancreatic necrosis was significantly better than that of patients with early infection and duration of organ failure before intervention was correlated with mortality of necrotizing pancreatitis. Despite the existence of infection, urgent intervention is unnecessary.

Author contributions

All of the authors contributed to the collection and analysis of the data and to the preparation of the report. The corresponding author had full access to all the data in the study and takes responsibility for the integrity of the data and the accuracy of the data analysis. All of the authors have seen and approved the final version of the Manuscript.

Disclosure

The authors declare no conflicts of interest and financial funding.

References

[1] Andersson B, Appelgren B, Sjödin V, Ansari D, Nilsson J, Persson U, et al. Acute pancreatitis–costs for healthcare and loss of production. Scand J Gastroenterol 2013;48:1459–65.
[2] Peery AF, Dellon ES, Lund J, Crockett SD, McGowan CE, Bulsiewicz WJ, et al. Burden of gastrointestinal disease in the United States: 2012 update. Gastroenterology 2012;143:1179–87.
[3] Besselink MG, van Santvoort HC, Buskens E, Boermeester MA, van Goor H, Timmerman HM, et al. Probiotic prophylaxis in predicted severe acute pancreatitis: a randomised, double-blind, placebo-controlled trial. Lancet 2008;371:651–9.
[4] Mazaki T, Ishii Y, Takayama T. Meta-analysis of prophylactic antibiotic use in acute necrotizing pancreatitis. Br J Surg 2006;93:674–84.
[5] Wu BU, Hwang JQ, Gardner TH, Repas K, Delee R, Yu S, et al. Lactated Ringer's solution reduces systemic inflammation compared with saline in patients with acute pancreatitis. Clin Gastroenterol Hepatol 2011;9:710–7.
[6] Besselink MG, van Santvoort HC, Boermeester MA, Nieuwenhuijs VB, van Goor H, Dejong CH, et al. Timing and impact of infections in acute pancreatitis. Br J Surg 2009;96:267–73.
[7] Beger HG, Bittner R, Block S, Büchler M. Bacterial contamination of pancreatic necrosis. A prospective clinical study. Gastroenterology 1986;91:433–8.
[8] van Baal MC, Bollen TL, Bakker OJ, van Goor H, Boermeester MA, Dejong CH, et al. The role of routine fine-needle aspiration in the diagnosis of infected necrotizing pancreatitis. Surgery 2014;155:442–8.
[9] Rau B, Pralle U, Mayer JM, Beger HG. Role of ultrasonographically guided fine-needle aspiration cytology in the diagnosis of infected pancreatic necrosis. Br J Surg 1998;85:179–84.
[10] Banks PA, Bollen TL, Dervenis C, Gooszen HG, Johnson CD, Sarr MG, et al. Classification of acute pancreatitis-2012: revision of the Atlanta classification and definitions by international consensus. Gut 2013;62:102–11.
[11] Isenmann R, Rau B, Beger HG. Early severe acute pancreatitis: characteristics of a new subgroup. Pancreas 2001;22:274–8.

[12] Sharma M, Banerjee D, Garg PK. Characterization of newer subgroups of fulminant and subfulminant pancreatitis associated with a high early mortality. Am J Gastroenterol 2007;102:2688–95.
[13] Johnson CD, Abu-Hilal M. Persistent organ failure during the first week as a marker of fatal outcome in acute pancreatitis. Gut 2004;53:1340–4.
[14] Lytras D, Manes K, Triantopoulou C, Paraskeva C, Delis S, Avgerinos C, et al. Persistent early organ failure: defining the high-risk group of patients with severe acute pancreatitis? Pancreas 2008;36:249–54.
[15] van Santvoort HC, Bakker OJ, Bollen TL, Besselink MG, Ahmed Ali U, Schrijver AM, et al. A conservative and minimally invasive approach to necrotizing pancreatitis improves outcome. Gastroenterology 2011;141:1254–63.
[16] Rodriguez JR, Razo AO, Targarona J, Thayer SP, Rattner DW, Warshaw AL, et al. Debridement and closed packing for sterile or infected necrotizing pancreatitis: insights into indications and outcomes in 167 patients. Ann Surg 2008;247:294–9.
[17] van Santvoort HC, Besselink MG, Bakker OJ, Hofker HS, Boermeester MA, Dejong CH, et al. N Engl J Med 2010;362:1491–502.
[18] Besselink MG, Verwer TJ, Schoenmaeckers EJ, Buskens E, Ridwan BU, Visser MR, et al. Timing of surgical intervention in necrotizing pancreatitis. Arch Surg 2007;142:1194–201.
[19] Guo Q, Li A, Xia Q, Liu X, Tian B, Mai G, et al. The role of organ failure and infection in necrotizing pancreatitis: a prospective study. Ann Surg 2014;259:1201–7.
[20] Mofidi R, Duff MD, Wigmore SJ, Madhavan KK, Garden OJ, Parks RW. Association between early systemic inflammatory response, severity of multiorgan dysfunction and death in acute pancreatitis. Br J Surg 2006;93:738–44.
[21] Working Group IAP/APA Acute Pancreatitis Guidelines. IAP/APA evidence-based guidelines for the management of acute pancreatitis. Pancreatology 2013;13(4 Suppl. 2):1–15.
[22] Baril NB, Ralls PW, Wren SM, Selby RR, Radin R, Parekh D, et al. Does an infected peripancreatic fluid collection or abscess mandate operation? Ann Surg 2000;231:361–7.
[23] Banks PA, Pappas TN. Is computerized tomographic fine needle aspiration helpful in the management of infected pancreatic necrosis? Am J Gastroenterol 2005;100:2371–4.
[24] Mofidi R, Lee AC, Madhavan KK, Garden OJ, Parks RW. Prognostic factors in patients undergoing surgery for severe necrotizing pancreatitis. World J Surg 2007;31:2002–7.