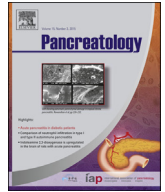




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Original article

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

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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.

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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

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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.

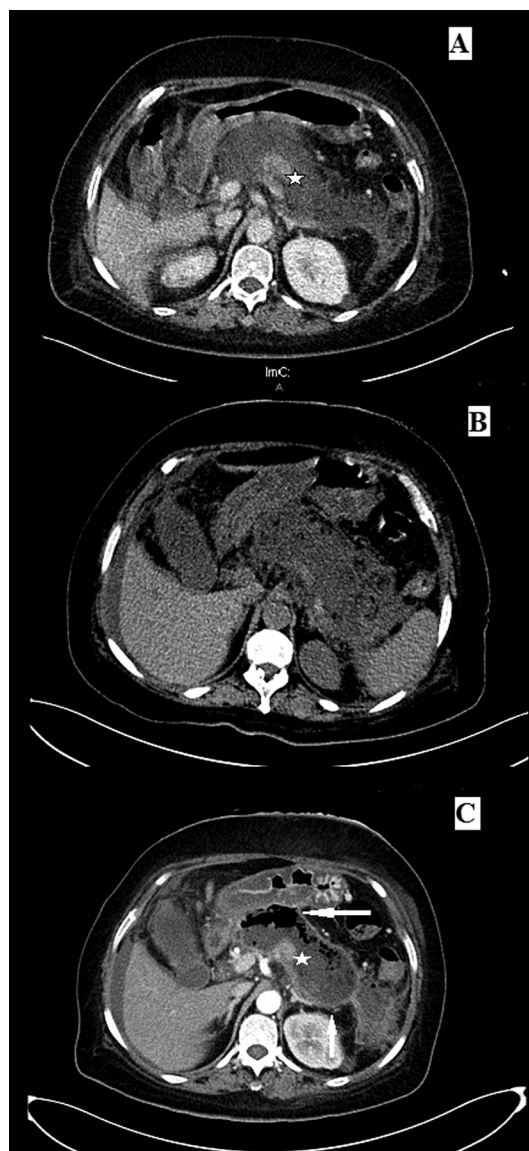


Fig. 1. (A) CECT scan of a 51 year-old female patient with acute pancreatitis 9 days after onset of symptoms. Normal enhancement of a part of the body of the pancreas (white asterisks) existed. (B) In unenhanced CT performed 23 days after onset, no gas bubbles were found. (C) About 32 days after onset, 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).

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