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Early on-demand drainage versus standard management in acute necrotizing pancreatitis with early persistent organ failure

Submission date
21/01/2020

Recruitment status
No longer recruiting

Registration date
23/01/2020

Overall study status
Completed

Last Edited
20/01/2022

Condition category
Digestive System

[_] Prospectively registered
[_] Protocol
[_] Statistical analysis plan
[X] Results
[_] Individual participant data

Plain English summary of protocol

Current plain English summary as of 10/06/2020:
Background and study aims
Acute necrotic collection (ANC) is one of the complications of acute pancreatitis, where death of pancreas cells which can develop into pus. In patients with persistent organ failure (POF), where the organ failure occurs for over 48 hours, the most severe type of pancreatitis, ANC is very common.

The current standard treatment for acute pancreatitis patients with ANC is to treat when the infection is suspected or confirmed and to postpone any invasive treatments for 4 weeks. However, the study team question if, in patients with POF, this delay may miss the opportunity to treat early infected ANC potentially leading to prolonged organ failure. The study team propose a novel early on-demand percutaneous drainage (PCD) approach using the persistent or worsening organ failure as an indication for drainage. PCD uses imaging guidance to place a needle or catheter through the skin into the ANC space to remove or drain the infected fluid.

The primary aim of this study is to assess the safety and outcomes of providing earlier PCD for patients with ANC and POF, based on the presence of persistent or worsening organ failure. This earlier approach will be compared to standard management. A secondary aim was to provide data for the design and power of a large-scale, multicenter, randomized, controlled trial

Who can participate?
Patients admitted to the center of severe acute pancreatitis (CSAP), Jinling Hospital during the study period were screened.

What does the study involve?
Patients are randomly allocated to either the early on-demand (EOD) catheter drainage group or the standard management group.

What are the possible benefits and risks of participating?
The current standard treatment for acute pancreatitis patients with ANC is to treat when the

infection is suspected or confirmed and to postpone any invasive treatments for 4 weeks. However, the study team question if, in patients with POF, this delay may miss the opportunity to treat early infected ANC potentially leading to prolonged organ failure. Patients with acute necrotizing pancreatitis and early POF may benefit from earlier on-demand catheter drainage to reduce complications and duration of organ failure.

Where is the study run from?
Jinling Hospital affiliated to Nanjing University (China). Initiated by the Chinese Acute Pancreatitis Clinical Trials Group (CAPCTG).

When is the study starting and how long is it expected to run for?
From June 2016 to December 2020

Who is funding the study?
Jiangsu Province Key Research and Development Program (Social Development) Project (China)

Who is the main contact?
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Previous plain English summary:
Background and study aims
Acute necrotic collection (ANC) is one of the complications of acute pancreatitis. In patients with persistent organ failure (POF), namely, the most severe type of AP patients, ANC is very common and it is controversial that if early invasive intervention before confirming infection is beneficial in this entity. Based on the previous studies, most ANC could be well absorbed or demarcated naturally, and percutaneous drainage may lead to bacterial colonization or infection of pancreatic necrosis. So it was suggested to delay intervention in asymptomatic patients. However, considering the pathophysiology of SAP, despite the sterile nature, ANC always contains numerous enzymes and inflammatory mediators, which play important roles in the development of POF and SIRS. It is controversial whether a delayed strategy in patients showing clinical deterioration before clear signs or evidence of infection is beneficial or could even worsen the outcomes. The aim of this study is to compare the effect of organ function-directed and infection-directed intervention in patients with ANC combined with POF (more than a week).

Who can participate?
All adult patients admitted with a primary diagnosis of acute pancreatitis and persistent organ failure to the participating hospital of the Chinese Acute Pancreatitis Clinical Trials Group will be assessed for eligibility on a daily basis during their hospital stay.

What does the study involve?
Patients are randomly allocated to receive either organ function-directed or infection-directed intervention.

What are the possible benefits and risks of participating?
Participants may get some clinical benefit from the trial and some advice from doctors.

Where is the study run from?
Jinling Hospital affiliated to Nanjing University (China)

Who is funding the study?
Jiangsu Province Key Research and Development Program (Social Development) Project (China)

Who is the main contact?
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Additional identifiers

Protocol serial number
2018NZKY-009-01

Study information

Scientific Title
The timing and indications for drainage in acute pancreatitis patients with acute necrotic collections and persistent organ failure: a pilot randomized controlled trial comparing early on-demand drainage and standard management

Study objectives
Current study hypothesis as of 10/06/2020:
For severe acute pancreatitis patients with acute necrotic collection and persistent organ failure in the early stages of disease, early on-demand percutaneous drainage could reduce mortality and major complications.

Previous study hypothesis as of 31/01/2020:
For severe acute pancreatitis patients complicated with acute necrotic collection and persistent organ failure in the early stages of disease, organ function-directed interventions may improve patient organ function and prognosis. This pilot study aimed to compare the effect of organ function-directed and infection-directed intervention.

Previous study hypothesis:
For severe acute pancreatitis patients complicated with acute necrotic collection and persistent organ failure in the early stages of disease, organ function-directed interventions may improve patient organ function and prognosis. This randomized, controlled, multi-center study aimed to compare the effect of organ function-directed and infection-directed intervention.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Current ethics approval as of 10/06/2020:
Approved 16/04/2018, Clinical trial ethics committee of the Jinling Hospital (305 Zhongshan Road East, Nanjing, Jiangsu, China; +861 (0)25-80863234; wuqiong80863234@163.com), ref: 2018NZKY-009-01

Previous ethics approval:
Approved 16/04/2018, Clinical trial ethics committee of the General Hospital of the Eastern Theater (305 Zhongshan Road East, Nanjing, Jiangsu, China; +861 (0)25-80863234; wuqiong80863234@163.com), ref: 2018NZKY-009-01

Study design
Randomized controlled single-blinded pilot trial

Primary study design
Interventional

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Acute pancreatitis

Interventions

Current interventions as of 16/06/2020:
All study subjects were randomized to either early on-demand (EOD) PCD group or the standard management group on Day 7 (The day of onset of abdominal pain was defined as Day 0).

Between randomization to Day 28 (intervention window, 21 days in total):
Patients who were randomized to the EOD group could receive PCD within the next 24 hours when one of the following criteria was met according to Modified Marshall Score:
1. Single or multiple organ systems failure (respiratory, renal and/or cardiovascular) unresolved for 7 days after randomization or;
2. New-onset organ failure arising after study Day 7 or;
3. Any worsening of any organ failure documented to be present on Day 7.

After placement, PCDs were audited by the investigators on a daily basis and were removed when the daily drainage volume was less than 50ml for three consecutive days and infection was not suspected or confirmed.

For the standard management group, interventions were postponed until 4 weeks after onset of abdominal pain whenever possible when infection was suspected or confirmed in line with current guidelines. PCD was also the primary choice of treatment in the standard management group

All the PCD procedures were performed by the same experienced team using 12F, 14F or 16F pig-tail catheters (UreSil, IL, US) in both groups, and the content drained from the site were cultured to determine whether it was sterile or infected. The size and numbers of drains placed was decided by the treating physicians.

Apart from timing and indication of drainage during the intervention window, all patients received standardized treatment according to the international guidelines including appropriate fluid resuscitation, early enteral nutrition, routine medical treatment like analgesics and proton-pump inhibitors if needed and organ support (e.g. mechanical ventilation, CRRT and vasoactive agent) as required. For infected pancreatic necrosis, once the diagnosis was made, all patients were managed with a step-up approach. Fine needle aspiration was not applied in this study and prophylactic antibiotics was avoided as well. Emergency surgery were indicated when active bleeding could not be controlled with arterial embolization, suspicion of bowel necrosis and gastrointestinal perforation leading to peritonitis occurred.

Previous interventions as of 31/01/2020:
Randomization will occur in a 1:1 fashion with computer-generated random numbers.

Organ function-directed group:
In addition to the standard treatment, ultrasound or CT guided percutaneous drainage would be applied once meeting one of the following conditions:
1. New-onset organ failure (no alleviation within 24 hours)
2. Unalleviated organ failure (either single or multiple, modified Marshall score ≥2) lasting for at least 7 days after randomization
3. Aggravation of organ failure from the baseline (either single or multiple) evidenced by increased modified Marshall score (no alleviation within 24 hours)

Infection-directed group:
Intervention including catheter drainage and necrosectomy would be delayed until suspicion or diagnosis of pancreatic infection and preferably after encapsulation of the necrotic collection (after 4 weeks mostly).

Previous interventions:
Randomization will occur in a 1:1 fashion for each center (sample size of each center was predefined based on its volume) with computer-generated random numbers.

Organ function-directed group:
In addition to the standard treatment, ultrasound or CT guided percutaneous drainage would be applied once meeting one of the following conditions:
1. New-onset organ failure (no alleviation within 24 hours)
2. Unalleviated organ failure (either single or multiple, modified Marshall score ≥2) lasting for at least 7 days after randomization
3. Aggravation of organ failure from the baseline (either single or multiple) evidenced by increased modified Marshall score (no alleviation within 24 hours)

Infection-directed group:
Intervention including catheter drainage and necrosectomy would be delayed until suspicion or diagnosis of pancreatic infection and preferably after encapsulation of the necrotic collection (after 4 weeks mostly).

Intervention Type
Procedure/Surgery

Primary outcome(s)
Current primary outcome measure as of 16/06/2020:
Death and/or major complications within 90 days after randomization. Major complications refer to: new-onset organ failure that was not present 24h before randomization; bleeding requiring intervention; and gastrointestinal perforation or fistulas requiring intervention. THese will be assessed using medical records, the Revised Marshall Score, diagnosis based on CT, bacterial culture results, or the symptoms of the patients. Multiple events that happened in the same patient were considered as one incidence of major complications.

Previous primary outcome measure:
1. All-cause mortality in hospital according to the medical records at the time of discharge
2. Major complications, including organ failure measured using Revised Marshall Score at baseline and daily during observation, complications such as infected pancreatic necrosis, sepsis, abdominal bleeding and fistulas according to diagnosis based on CT, bacterial culture results or the symptoms of the patients

Key secondary outcome(s))
Current secondary outcome measures as of 16/06/2020:
1. Incidence of each of the individual components of death and the major complications listed in the primary outcome measure within 90 days after randomization
2. Incidence of infected pancreatic necrosis according to diagnosis based on CT, bacterial culture results, or the symptoms of the patient within 90 days after randomization
3. Incidence of sepsis according to SEPSIS 3.0 definition within 90 days after randomization
4. Incidence of external pancreatic fistula according to diagnosis based on CT, drainage, or the symptoms of the patient within 90 days after randomization

5. New receipt of organ support taken from the medical records at the time of discharge
6. The requirement for PCD, minimally invasive necrosectomy, open surgery, reoperation taken from the medical records at the time of discharge
7. Total number of PCD and minimally invasive necrosectomy procedures taken from the medical records at the time of discharge
8. The duration of organ failure and organ support between randomization and Day 28 (21 days in total) taken from the medical records at the time of discharge
9. Total expense taken from billing system at the time of discharge
10. Death by 180 days after randomization based on an additional follow-up

Previous secondary outcome measures:
1. Incidence and timing of infected pancreatic necrosis according to diagnosis based on CT, bacterial culture results or the symptoms of the patients
2. Incidence and timing of sepsis according to diagnosis based on CT, bacterial culture results or the symptoms of the patients
3. Incidence and timing of other common complications such as abdominal bleeding and fistulas according to diagnosis based on CT or the symptoms of the patients
4. Requirement of open surgery taken from the medical records at the time of discharge
5. ICU duration taken from the medical records at the time of discharge
6. Hospital duration taken from the medical records at the time of discharge
7. Total cost taken from billing system at the time of discharge

Completion date
31/12/2020

Eligibility

Key inclusion criteria
Current participant inclusion criteria as of 16/06/2020:
1. Symptoms and signs of acute pancreatitis based on abdominal pain suggestive of AP, serum amylase at least three times the upper limit of normal, and/or characteristic findings of AP on computed tomography
2. Admitted within 7 days from onset of abdominal pain
3. Confirmed persistent organ failure (respiratory, circulatory, renal) failure (revised Marshall score ≥ 2 points for at least 48 h) and still unresolved 7 days after onset
4. Age between 18 to 70 years old
5. Acute necrotic collection with available routes for ultrasound or CT guided percutaneous drainage

Previous participant inclusion criteria:
1. Symptoms and signs of acute pancreatitis based on abdominal pain suggestive of AP, serum amylase at least three times the upper limit of normal, and/or characteristic findings of AP on computed tomography
2. The duration of disease up to 1 week (starting with abdominal pain)
3. Confirmed persistent organ failure (respiratory, circulatory, renal) failure (revised Marshall score ≥ 2 points and the duration of up to 48 hours)
4. Age between 18 to 70 years old
5. Necrotic collection with available routes for ultrasound or CT guided percutaneous no matter sterile or infected

Participant type(s)

Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex
All

Total final enrolment
30

Key exclusion criteria
Current participant exclusion criteria as of 16/06/2020:
1. Pregnancy
2. Chronic pancreatitis or pancreatic tumor-related pancreatitis
3. Percutaneous or transluminal drainage or surgery undertaken before admission
4. Previous history of cardio-pulmonary resuscitation during the present admission for AP
5. Expected to die within 48 h
6. Emergency surgery required due to active bleeding, bowel ischemia or necrosis, etc.
7. History of severe co-morbidities:
7.1. Greater than New York Heart Association class II heart failure
7.2. Active myocardial ischemia
7.3. History of cirrhosis
7.4 Chronic kidney disease with creatinine clearance <40 mL/min
7.5 Chronic obstructive pulmonary disease requiring home oxygen

Previous participant exclusion criteria:
1. Pregnant
2. Chronic pancreatitis, recurrent acute pancreatitis or pancreatic tumor-related pancreatitis
3. Percutaneous or transluminal drainage or surgery undertaken before admission
4. Previous history of cardio-pulmonary resuscitation
5. History of severe cardiovascular, respiratory, renal, hepatic, hematologic, or immunologic disease defined as:
5.1. Greater than New York Heart Association class II heart failure
5.2. Active myocardial ischemia
5.3. Cardiovascular intervention within the previous 60 days
5.4. History of cirrhosis
5.5 Chronic kidney disease with creatinine clearance< 40 mL/min
5.6 Chronic obstructive pulmonary disease with requirement for home oxygen

Date of first enrolment
02/07/2018

Date of final enrolment
12/08/2019

Locations

Countries of recruitment
China

Study participating centre
Jinling Hospital affiliated to Nanjing University
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Sponsor information

Organisation
Jinling Hospital affiliated to Nanjing University

Funder(s)

Funder type
Government

Funder Name
Jiangsu Province Key Research and Development Program (Social Development) Project (BE2016749)

Results and Publications

Individual participant data (IPD) sharing plan
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

Previous publication and dissemination plan:
Planned publication in a high-impact peer-reviewed journal.

IPD sharing statement
The datasets generated and/or analysed during the current study during this study will be included in the subsequent results publication.

IPD sharing plan summary

Other

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		18/03/2021	20/01/2022	Yes	No