ISRCTN91106416 https://doi.org/10.1186/ISRCTN91106416

Early on-demand drainage versus standard management among acute necrotizing pancreatitis patients complicated by persistent organ failure

Submission date
17/10/2019

Recruitment status
No longer recruiting

Registration date
21/10/2019

Overall study status
Completed

Last Edited
18/06/2020

Condition category
Digestive System

[ ] Prospectively registered
[ ] Protocol
[ ] Statistical analysis plan
[ ] Results
[ ] Individual participant data
[ ] Record updated in last year

Plain English summary of protocol

Background and study aims
Sometimes people with severe acute pancreatitis can develop a complication where the pancreas loses its blood supply. This can cause some of the tissue of the pancreas to die (necrosis). When this happens, the pancreas can become infected, which can spread into the blood (sepsis) and cause organ failure. People with necrosis and an infection may need injections of antibiotics and surgery to remove the dead tissue. This is a very serious complication that needs treating, and it can be fatal. The study aims to compare standard treatment with a standard treatment preceded by fluid drainage immediately upon diagnosis.

Who can participate?
All adult patients admitted with a primary diagnosis of acute pancreatitis and persistent organ failure to one of the five participating hospitals 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 will be randomised to receive either immediate drainage followed by standard treatment, or standard treatment.

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

Where is the study run from?
1. Jinling Hospital affiliated to Nanjing University (the lead center)
2. The First Affiliated Hospital of Nanchang University
3. Xiang Ya hospital Zhongnan University
4. Sir Run Run Shaw Hospital affiliated with the Zhejiang University School of Medicine
5. Xijin Hospital, of the Fourth Military Medical University

When is the study starting and how long is it expected to run for?
March 2019 March 2022

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

Who is the main contact?
1. Dr Qu Cheng
njumedqc@163.com
2. Dr Ke Lu
kkb9832@gmail.com

Contact information

Type(s)
Public

Contact name
Mr Qu Cheng

ORCID ID
https://orcid.org/0000-0002-0822-5074

Contact details
305 Zhongshan Road East
Nanjing
China
210000
+8618862879105
njumedqc@163.com

Additional identifiers

Clinical Trials Information System (CTIS)
Nil known

ClinicalTrials.gov (NCT)
Nil known

Protocol serial number
2018NZKY-009-04

Study information

Scientific Title
Early on-demand drainage versus standard management among acute necrotizing pancreatitis patients complicated by persistent organ failure: an open-label multicenter randomized controlled trial

Acronym

TIMING

Study objectives
Current study hypothesis as of 18/06/2020:
Early percutaneous drainage in selected patients with acute necrotizing pancreatitis (ANC) and persistent organ failure (POF), who have aggravating or long-lasting organ failure during week 2-3 will result in improved clinical outcomes. We called this an on-demand approach for short. This will be tested in this randomized, controlled, multi-center study, aiming to compare the effect of the early on-demand drainage of ANC and standard treatment (delayed intervention).

Previous study hypothesis:
Early percutaneous drainage in selected patients with acute necrotizing pancreatitis (ANC) and persistent organ failure (POF), who have aggravating or long-lasting organ failure during week 2-3 will result in improved clinical outcomes. We called this an on-demand approach for short. This will be tested in this randomized, controlled, multi-center study, aiming to compare the effect of the early on-demand intervention of ANC and standard treatment (delayed intervention)

Ethics approval required
Old ethics approval format

Ethics approval(s)
Current ethics approval as of 18/06/2020:
Approved 29/11/2018, Clinical trial ethics committee of the Jinling hospital (305 Zhongshan Road East, Nanjing, Jiangsu, China; wuqiong80863234@163.com; +861 (0)25-80863234), ref: 2018NZKY-009-04

Previous ethics approval:
Approved 29/11/2018, Clinical trial ethics committee of the General Hospital of the Eastern Theater (305 Zhongshan Road East, Nanjing, Jiangsu, China; wuqiong80863234@163.com; +861 (0)25-80863234), ref: 2018NZKY-009-04

Study design
Multi-center randomized controlled open-label trial

Primary study design
Interventional

Study type(s)
Treatment

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

Interventions
Current interventions as of 18/06/2020:
This randomized, controlled, multi-center study, aims to compare the effect of the early on-demand drainage of ANC and standard treatment (delayed intervention)

Early on-demand PCD group (the EOD group):
In addition to the standard treatment, ultrasound or computed tomography(CT) guided PCD will be performed within 24 hours of randomization. Early on demand endoscopic drainage is not

permitted in this arm, as we can not monitor daily volume of the endoscopic drain. At least one drainage catheter with size from 12F to 16F will be placed to drain the ANC, and the content drained from the site will be cultured to determine whether it is sterile or infected. More drains are permitted if deemed clinically necessary based on patient status and extent of the collection. The treating physician is responsible for choosing the access routes, size, and the number of drains. The percutaneous drains will be audited every day and removed to reduce the unnecessary risk for introducing infection when the volume of a given catheter is less than 50ml (including 50ml) for three consecutive days and infection has not been suspected or confirmed. Debridement of the infected necrosis (necrosectomy) will be performed once there is encapsulation and as scheduled by the treating physician. For minimally-invasive techniques, both percutaneous and endoscopic necrosectomy are acceptable based on the technical preference and availability within each participating center.

Standard-care group (the standard group):
No intervention will be immediately applied if the participant is randomized to this group unless meeting the “rescue intervention criteria” shown below. Interventions, including PCD and necrosectomy, will be delayed until high suspicion or diagnosis of infection associated with WON and preferably at least four weeks following admission. Both percutaneous drainage and endoscopic transluminal drainage can be selected for the initial step, and necrosectomy would be undertaken when necessary.

Previous interventions:
This randomized, controlled, multi-center study, aims to compare the effect of the early on-demand intervention of ANC and standard treatment (delayed intervention)

Early intervention:
In addition to the standard treatment, ultrasound or CT guided percutaneous drainage would be applied within 24 hours once the patient is randomized to this group. At least one drainage catheter with size from 12F to 16F should be placed to drain the ANC, the content drained from the site will be tested by the standard procedure to detect potential infection (more drains are permitted). The treating physician is responsible for choosing the access routes, size and number of catheters.

Standard-treatment:
No intervention would be immediately applied if the participant is randomized to this group. Interventions including catheter drainage and necrosectomy would be delayed until suspicion or diagnosis of pancreatic infection and preferably after encapsulation of the necrotic collection (after four weeks for the best).

Patients will be randomly allocated to receive early intervention, within 24 hours after randomization, or standard treatment (delayed strategy) according to the current guidelines. Patients are randomized (1:1 ratio within each participating center and sample size of each center was predefined based on its volume) with a web-based randomization module (Interactive Web-Respond System (IWRS).

Intervention Type
Procedure/Surgery

Primary outcome(s)
Current primary outcome measure as of 18/06/2020:
Death and/ or major complications during the index admission from randomization to hospital discharge or death. Major complications refer to new-onset organ failure (cardiovascular, renal

and respiratory), bleeding requiring intervention and gastrointestinal perforation or fistula requiring intervention.

Previous primary outcome measure:
1. All-cause mortality in hospital
2. Major complications during the observational period

Key secondary outcome(s))
Current secondary outcome measures as of 18/06/2020:
1. New-onset organ failure before the time of hospital discharge or death
2. Bleeding requiring intervention before the time of hospital discharge or death
3. Gastrointestinal perforation or fistula requiring intervention before the time of hospital discharge or death
4. Deteriorated organ failure before the time of hospital discharge or death
5. Organ failure score assessed at 14 and 21 days after randomization
6. Organ failure-free days during the 21-day period following randomization
7. Intra-abdominal pressure for seven consecutive days after randomization and 14, 21 days after randomization
8. Incidence of infected pancreatic necrosis before the time of hospital discharge or death
9. Incidence of sepsis before the time of hospital discharge or death
10. New prescription of mechanical ventilation, renal replacement therapy and vasoactive agents before the time of hospital discharge or death
11. Incidence of pancreatic fistula before the time of hospital discharge or death
12. Incidence of symptomatic splenic vein thrombosis before the time of hospital discharge or death
13. Requirement of minimally inv supraventricular tachycardia asive debridement before the time of hospital discharge or death
14. Requirement of open surgery before the time of hospital discharge or death
15. Duration of ICU admission before the time of hospital discharge or death
16. Duration of hospital admission before the time of hospital discharge or death
17. Total cost before the time of hospital discharge or death
18. Vital status on 90 days after randomization

Previous secondary outcome measures:
1. The fluctuation of organ functions reflected by the area under curve according to the revised Marshall score for seven consecutive days after randomization
2. Organ function assessed by revised Marshall at 14 and 21 days after randomization if available
3. Intraabdominal pressure for seven consecutive days after randomization and 14, 21 days after randomization if available
4. Incidence and timing of infected pancreatic necrosis
5. Incidence and timing of sepsis
6. Incidence and timing of other common complications such as abdominal bleeding and fistulas
7. Requirement of open surgery
8. ICU duration
9. Hospital duration
10. Total cost

Completion date
01/06/2022

Eligibility

Key inclusion criteria
Current inclusion criteria as of 18/06/2020:
1. Aged 18 to 70 years
2. Able to provide informed consent
3. Confirmed diagnosis of AP
4. CT diagnosis of acute necrotic collection (ANC)
5. Technically able to be drained percutaneously, by ultrasound or CT guidance
6. Confirmed persistent organ failure (either respiratory, renal and/or cardiovascular lasting for more than 48 hours) that had not resolved by Day 7
7. During Day 8-Day 21, one or more of these criteria:
7.1. New-onset organ failure not present on Day 7 (no alleviation within 24 hours)
7.2. Organ failure (either single or multiple, modified Marshall score or SOFA score≥2) persist for seven natural days from Day 1
7.3. Aggravation of organ failure from that on Day 7 evidenced by increased modified Marshall score or SOFA score (no alleviation within 24 hours)

Previous inclusion criteria:
Inclusion criteria for the screening period
Screening period starts from day 8 and extends to the end of the third week (day 21) consisting of 14 days:
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. Necrotic collection with available routes for ultrasound or CT guided percutaneous no matter sterile or infected
3. Confirmed persistent organ failure (either respiratory, renal or cardiovascular lasting for more than 48 hours), the organ failure score at day7 will be set as the baseline for the screening period
4. Age between 18 to 70 years old

Inclusion Criteria for randomization during screening period:
1. Patients in the screening period
2. Signs of deterioration from the baseline during the screening period including:
2.1. New-onset organ failure (no alleviation within 24 hours)
2.2. Unalleviated organ failure (either single or multiple, modified Marshall score≥2) lasting for at least seven days including the duration before the screening period
2.3. Aggravation of organ failure from the baseline (either single or multiple) evidence by increased modified Marshall score (no alleviation within 24 hours)

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 years

Sex

All

Key exclusion criteria
Current exclusion criteria as of 18/06/2020:
1. Pregnant pancreatitis
2. Chronic pancreatitis
3. Pancreatic tumor-related pancreatitis
4. Percutaneous or transluminal drainage or surgery is undertaken before admission
5. Patients had a history of cardio-pulmonary resuscitation during this episode
6. Patients with a known history of severe cardiovascular, respiratory, renal or hepatic disease defined as (1) greater than New York Heart Association class II heart failure, (2) active myocardial ischemia or (3) cardiovascular intervention within previous 60 days, (4) history of cirrhosis or (5) chronic kidney disease with creatinine clearance< 40 mL/min, or (6) chronic obstructive pulmonary disease with requirement for home oxygen

Previous 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
01/03/2019

Date of final enrolment
01/03/2022

Locations

Countries of recruitment
China

Study participating centre
Jinling Hospital affiliated to Nanjing University
305 Zhongshan Road East
Nanjing
China
210000

Study participating centre
The First Affiliated Hospital of Nanchang University
17 Yongwaizheng street
Nanchang
China
330000

Study participating centre
Xiang Ya hospital Zhongnan University
87 Xiangya Road
Changsha
China
410000

Study participating centre
Sir Run Run Shaw Hospital affiliated with the Zhejiang University School of Medicine
3 Qingchun East Road
Jianggan District
Hangzhou
China
310000

Study participating centre
Xijin Hospital of the Fourth Military Medical University
127 Changle West Road
Xincheng District
Xi'an City
Xian
China
710000

Sponsor information

Organisation
Department of science and technology of Jiangsu province

ROR
https://ror.org/02mkqta53

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
All data generated or analysed 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?
Participant information sheet	Participant information sheet	11/11/2025	11/11/2025	No	Yes
Study website	Study website	11/11/2025	11/11/2025	No	Yes