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Investigating the effectiveness of early detection and treatment of bile duct stones in acute gallstone pancreatitis

Submission date
28/08/2018

Recruitment status
No longer recruiting

Registration date
10/09/2018

Overall study status
Completed

Last Edited
28/02/2023

Condition category
Digestive System

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

Plain English summary of protocol

Background and study aims
Acute biliary pancreatitis is inflammation of the pancreas caused by obstruction of the pancreatic duct. Relieving the obstruction early with an operation called endoscopic retrograde cholangiography (ERC) with endoscopic sphincterotomy (ES) may be beneficial, especially if this condition is persistent. The aim of this study is to investigate whether early detection of common bile duct obstruction followed by direct treatment of such an obstruction with ERC plus ES, reduces complications and/or the number of deaths in patients with acute biliary pancreatitis.

Who can participate?
Adult patients with acute biliary pancreatitis

What does the study involve?
Participants are treated with early EUS (endoscopic ultrasound) (within 24 hours of admission to hospital) followed by direct ERC plus ES, if they have sludge and/or gallstones in their common bile duct.

What are the possible benefits and risks of participating?
Patients with sludge and/or gallstones in the common bile duct may benefit from undergoing ERC plus ES, as early clearance of the obstruction can be beneficial. In patients without biliary obstruction, unnecessary ERC plus ES can be prevented. The potential risk of participating is that the ERC plus ES procedure may lead to complications in a minority of patients; however, there are several safety procedures and evaluation moments to guarantee the patients' safety throughout the study. These complications include bleeding, bowel perforation, cholangitis and aspiration pneumonia; however, these complications occur in around 1% of cases.

Where is the study run from?
Erasmus Medical Center (The Netherlands) and 18 participating centres in the Netherlands

When is the study starting and how long is it expected to run for?
June 2017 to September 2019

Who is funding the study?
Erasmus Medical Center (The Netherlands)

Who is the main contact?
Prof. M.J. Bruno
m.bruno@erasmusmc.nl

Study website
https://pancreatitis.nl/studies/apec

Contact information

Type(s)
Scientific

Contact name
Prof M.J. Bruno

Contact details
Erasmus Medical Center
Department of Gastroenterology and Hepatology
Doctor Molewaterplein 40
Rotterdam
Netherlands
3015 GD

Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers
MEC-2012-357

Study information

Scientific Title
EUS-guided early ERC with sphincterotomy in predicted severe biliary pancreatitis: a prospective, multicenter cohort study with a historic comparison

Acronym
APEC-2

Study objectives

We hypothesise that endoscopic ultrasonography (EUS)-guided early endoscopic retrograde cholangiography (ERC) with sphincterotomy improves the outcome of patients with acute biliary pancreatitis without cholangitis, in whom the disease course is predicted to be severe.

Ethics approval required
Old ethics approval format

Ethics approval(s)
Erasmus Medical Center Rotterdam Ethics Committee, 27/06/2017 ref: MEC-2012-357

Study design
Interventional prospective multi-centre non-randomised cohort study

Primary study design
Interventional

Secondary study design
Non randomised study

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Patient information can be found at https://pancreatitis.nl/studies/apec

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

Interventions
The study will be performed by the Dutch Pancreatitis Study Group. A total of 78 evaluable patients will be included in 18 participating centers. This group will receive early (<24 hours of admission) endoscopic ultrasound, followed by direct endoscopic retrograde cholangiography (ERC) with sphincterotomy if they have sludge or gallstones in the common bile duct. This will be compared with a historic cohort (the superior group of the APEC trial (ISRCTN97372133)). If the APEC trial shows no difference between the two groups, the conservative group or the early ERC with sphincterotomy group, a comparison will be made between the EUS group and the conservative group.
There will be a 6 month follow-up period, which will involve participants filling in questionnaires 1, 3 and 6 months after inclusion. 3 months after inclusion there will be a follow-up visit at the outpatient clinic to assess liver and pancreatic function.

Intervention Type
Procedure/Surgery

Primary outcome measure
Composite of severe morbidity and mortality occurring until 6 months after inclusion. Severe morbidity is defined as the occurrence of persistent single organ failure, necrotizing

pancreatitis, bacteremia, cholangitis, pneumonia or exocrine or endocrine pancreatic insufficiency. After patient inclusion is completed and after the last patient has completed the 6 month follow-up, an adjudication committee consisting of 4 gastroenterologists, 2 surgeons and 1 radiologist will assess all potential endpoints (i.e. mortality and severe complications) and decide whether these concord with definitions of the primary endpoints. Using primary source data, each member of the committee will individually assess the potential endpoints. Disagreements will be resolved at a plenary consensus meeting.

Secondary outcome measures
The following are assessed at 6 month follow-up. For the secondary endpoints three sources of data are used: clinical record forms that are filled out by the treating physicians, primary source data and questionnaires filled out by the patients at 1,3 and 6 month follow-up.
1. Individual components of the primary endpoint
2. Length of hospital stay
3. Need for of new intensive care admission
4. Length of intensive care stay
5. Respiratory complications
6. Endoscopic retrograde cholangiography (ERC) related complications
7. Number of endoscopic, radiological and operative (re-)interventions
8. Readmission for biliary events
9. Difficulty of cholecystectomy
10. Economical evaluation

Overall study start date
27/06/2017

Completion date
01/09/2019

Eligibility

Key inclusion criteria
1. Acute biliary pancreatitis
2. Predicted severe disease course
3. EUS and ERC with sphincterotomy can be performed within 24 hours after admission
4. Aged 18 years or older
5. Written informed consent
6. In case of a previous episode of necrotizing pancreatitis, patient should be fully recovered

Participant type(s)
Patient

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
78 evaluable patients

Total final enrolment
83

Key exclusion criteria
1. Cholangitis
2. Acute pancreatitis due to other causes such as alcohol abuse, metabolic causes, medication, trauma, etc.
3. Previous (precut) sphincterotomy
4. Chronic pancreatitis
5. International Normalised Ratio (INR) that cannot be corrected with co-fact or fresh frozen plasma below 1.5
6. Pregnancy

Date of first enrolment
15/08/2017

Date of final enrolment
01/03/2019

Locations

Countries of recruitment
Netherlands

Study participating centre
Erasmus Medical Center
Doctor Molewaterplein 40
Rotterdam
Netherlands
3015 GD

Study participating centre
Albert Schweitzer Hospital
Albert Schweitzerplaats 25
Dordrecht
Netherlands
3318 AT

Study participating centre
Amphia Hospital
Molengracht 21
Breda

Netherlands
4818 CK

Study participating centre
Amsterdam University Medical Centers location AMC
Meibergdreef 9
Amsterdam
Netherlands
1105 AZ

Study participating centre
Amsterdam University Medical Centers location VUmc
De Boelelaan 1117
Amsterdam
Netherlands
1081 HV

Study participating centre
Elisabeth Tweesteden Hospital
Doctor Deelenlaan 5
Tilburg
Netherlands
5042 AD

Study participating centre
Erasmus Medical Center
Doctor Molewaterplein 40
Rotterdam
Netherlands
3015 GD

Study participating centre
Franciscus Gasthuis
Kleiweg 500
Rotterdam
Netherlands
3045 PM

Study participating centre

Gelre Hospital
Albert Schweitzerlaan 31
Apeldoorn
Netherlands
7334 DZ

Study participating centre
Isala Klinieken
Dokter van Heesweg 2
Zwolle
Netherlands
8025 AB

Study participating centre
Martini Hospital
Van Swietenplein 1
Groningen
Netherlands
9728 NT

Study participating centre
Meander Medical Center
Maatweg 3
Amersfoort
Hoogland
Netherlands
3813 TZ

Study participating centre
Medisch Spectrum Twente
Koningsplein 1
Enschede
Netherlands
7512 KZ

Study participating centre
Onze Lieve Vrouwe Gasthuis
Oosterpark 9
Amsterdam
Netherlands
1091 AC

Study participating centre
Radboud University Medical Center
Geert Grooteplein Zuid 10
Nijmegen
Netherlands
6525 GA

Study participating centre
Reinier de Graaf Hospital
Reinier de Graafweg 5
Delft
Netherlands
2625 AD

Study participating centre
Spaarne Gasthuis
Boerhaavelaan 22
Haarlem
Netherlands
2035 RC

Study participating centre
St Antonius Hospital
Koekoekslaan 1
Nieuwegein
Netherlands
3435 CM

Study participating centre
Gelderse vallei Hospital
Willy Brandtlaan 10
Ede
Netherlands
6716 RP

Sponsor information

Organisation
Erasmus Medical Center

Sponsor details
Doctor Molewaterplein 40,
Rotterdam
Netherlands
3015 GD

Sponsor type
Hospital/treatment centre

Website
www.erasmusmc.nl

ROR
https://ror.org/018906e22

Funder(s)

Funder type
Not defined

Funder Name
Investigator initiated and funded

Results and Publications

Publication and dissemination plan
Planned publication in a high-impact peer-reviewed journal

Intention to publish date
01/06/2022

Individual participant data (IPD) sharing plan
All requests for access to data generated as a result of this study should be send to M.J. Bruno (m.bruno@erasmusmc.nl) and will be reviewed by the board of the Dutch Pancreatitis Study Group to ensure scientific integrity and data protection.

IPD sharing plan summary
Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		27/02/2023	28/02/2023	Yes	No