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	 Prospectively registered Protocol
Registration date 10/09/2018	Overall study status Completed	 [] Statistical analysis plan [X] Results
Last Edited 28/02/2023	Condition category Digestive System	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

Cholangitis
 Acute pancreatitis due to other causes such as alcohol abuse, metabolic causes, medication, trauma, etc.
 Previous (precut) sphincterotomy
 Chronic pancreatitis
 International Normalised Ratio (INR) that cannot be corrected with co-fact or fresh frozen plasma below 1.5
 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?
Results article		27/02/2023	28/02/2023	Yes

Patient-facing? No