Acute biliary Pancreatits: early ERC plus sphincterotomy versus Conservative treatment: the APEC trial, a randomized, superiority, assessor-blinded multicenter trial.

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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Exocrine pancreas conditions
Study type	Interventional

Summary

ID

NL-OMON45093

Source
ToetsingOnline

Brief title
APEC trial

Condition

- Exocrine pancreas conditions
- Bile duct disorders
- Gastrointestinal therapeutic procedures

Synonym
Biliary pancreatitis / galstone induced acute inflammation of the pancreas

Research involving

Human

Sponsors and support

Primary sponsor: Erasmus MC, Universitair Medisch Centrum Rotterdam
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: - biliary pancreatitis, - endoscopische retrograde cholangio(pancreatico)graphy (ERC(P)), - sphincterotomy, Endoscopic Ultrasonography (EUS)

Outcome measures

Primary outcome

Incidence of a composite endpoint of mortality and severe complications.

Major Complications are considered as (for definitions see protocol Appendix

Table 3):

- organ failure

- pancreatic necrosis

- bacteremia

- cholangitis

- pneumonia

- exocrine and/ or endocrine pancreatic insufficiency

Secondary outcome

Incidence of all individual components of the primary endpoint, length of

hospital stay, new onset intensive care admission, length of intensive care

stay, respiratory complications, cholangitis during admission, ERC-related

complications, number of endoscopic, radiological and operative (re-)

interventions, readmission for biliary events, difficulty of cholecystectomy

and cost-effectiveness with direct medical and non-medical and indirect costs.

Study description

Background summary

Acute biliary pancreatitis (ABP) is a serious illness with an overall mortality rate ranging from 1% for mild pancreatitis to around 20% for infected necrotizing pancreatitis. In the majority of cases the causative and initiating events are passage and impaction of biliary stones and sludge in the common bile duct and ampulla. Early relief of obstruction and removal of stones and sludge by endoscopic retrograde cholangiography (ERC) and endoscopic sphincterotomy (ES) may prevent the disease to deteriorate to (infected) necrotizing pancreatitis, thereby reducing mortality and morbidity rates substantially.

Study objective

The objective of the study is to investigate whether early ERC plus ES in patients with suspected APB and a predicted severe disease course without cholangitis, lowers the incidence of a composite endpoint of mortality and severe morbidity. Major morbidity is further discussed under the heading "primary and secondary endpoints".
Furthermore this study investigates if the addition of a diagnostic EUS, followed by ERC with ES in case of gallstones/sludge can further reduce the composite endpoint.

Study design

Randomized, superiority, assessor-blinded multicenter trial with a follow-up of 6 months after randomisation for primary and secondary endpoints, followed by a prospective multicenter cohort with a similar protocol and follow-up.

Intervention

Intervention: Early (<24 hrs after admission and < 72 hrs after start symptoms) ERC plus ES.
Comparison: Conservative (expectative) management with delayed intervention only when clinically indicated.

Prospective cohort: Early (<24 hrs after admission and < 72 hrs after start symptoms) EUS-guided ERC with ES

Study burden and risks

Patients included in the early ERC plus ES group are exposed to the normal complications associated with an ERC with ES. ERC's will carried out by, or under direct supervision of, an experienced interventional endoscopist. Complications which might occur are performation, bleeding, respiratory insufficiëncy, cardiovascular complications or the development of a post-ERC pancreatitis. Patients allocated to conservative treatment will not undergo early ERC unless he/ she develops a cholangitis. To date no adequately designed trial has been performed to definitely define the role of ERC plus ES in patients with a predicted severe acute biliary pancreatitis. Estimated beneficial risks of ERC in proportion to the normal ERC-related complications are difficult to assess. However, the hypothesis is that an early ERC plus ES ameloriates the disearse course. To prove this a randomised controlled clinical trial is urgently needed.

Experimental studies indicate that only in case of mechanical obstruction of the ampulla, an ERC with sphincterotomy can be usefull. Patients in whom gallstones/sludge have passed into the duodenum spontaneously probably have no benefit form this intervention. EUS can reliably evaluate the presence of gallstones/sludge in de common bile duct and has recently become available in most Dutch hospitals. Investigating if early EUS-guided ERC with ES in this patient population can further ameliorate the treatment compared to conservative treatment or ERC with ES is indicated. EUS can on the one hand potentially reduce the amount of ERC procedures and their accompanying procedural risks and can on the other hand warrant direct treatment for patients with visible common bile duct obstruction.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

1. Acute pancreatitis, defined as the presence of at least 2 out of the following 3 criteria:
- upper abdominal pain
- serum amylase and/ or lipase concentration >3 times the upper limit of normal
- signs of pancreatitis on CT or MR
2. Predicted severe course of the acute pancreatitis based on either one of the following positieve scores:
- CRP >150mg/L
- Imrie score * 3
- APACHE II score * 8
3. High probability acute biliary pancreatitis: see criterion 1 and at least one of the following criteria:
- gallstones and/ or biliary sludge on imaging (US, CT of MR)
- a dilated common bile duct on imaging (US, CT of MR) defined as >8mm in patients * 75 years or >10mm in patients >75 years
- ALAT > two times upper limit of normal
4. ERC can be performed within 24 hours after admission, but no more than 72 hours after the start of symtoms
5. Age >18 year old
6. Written informed consent
7. In case of a previous episode of necrotizing pancreatitis, patient should be fully recovered (confirmed on imaging)

Exclusion criteria

1. Cholangitis
2. Acute pancreatitis due to other causes such as alcohol abuse (either chronic or binge drinking), metabolic causes, medication, trauma, etc.

3. Pregnancy
4. Previous precut sphincterotomy and/ or ES
5. INR that cannot be corrected with co-fact or FFP below 1.5
6. Chronic pancreatitis

Study design

Design

Study type:	Interventional
Intervention model:	Other
Allocation:	Randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Health services research

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	01-03-2013
Enrollment:	310
Type:	Actual

Ethics review

Approved WMO Date:	12-12-2012
Application type:	First submission
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	09-05-2014
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Approved WMO Date:	09-06-2015
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	27-06-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)
Approved WMO Date:	11-12-2017
Application type:	Amendment
Review commission:	METC Erasmus MC, Universitair Medisch Centrum Rotterdam (Rotterdam)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

No registrations found.

In other registers

Register	ID
ISRCTN	ISRCTN97372133
CCMO	NL39745.078.12