SpHincterotomy for Acute Recurrent Pancreatitis

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The hypothesis is that obstruction at the level of the minor papilla is one cause of RAP in pancreas divisum; miES will relieve the obstruction, thereby reducing the risk of a recurrent attack(s) of acute pancreatitis.

Ethical review	Approved WMO
Status	Pending
Health condition type	Gastrointestinal therapeutic procedures
Study type	Interventional

Summary

ID

NL-OMON48117

Source
ToetsingOnline

Brief title
SHARP-trial

Condition

- Gastrointestinal therapeutic procedures

Synonym
Pancreas divisum

Research involving
Human

Sponsors and support

Primary sponsor: Medical University of South Carolina
Source(s) of monetary or material Support: Ministerie van OC&W

Intervention

Keyword: Acute pancreatitis, ERCP, Pancreas divisum, sphincterotomy

Outcome measures

Primary outcome

1.Reduce the risk of subsequent acute pancreatitis:

To test this aim, compare the incidence of acute pancreatitis > 30 days after

treatment allocation as the primary outcome measure, using the next attack of

acute pancreatitis as a time-to-event outcome.

Secondary outcome

Incidence rate ratio.

Patient-reported outcomes

Progression to chronic pancreatitis

Biorepository

Study description

Background summary

ERCP is a moderately high-risk intervention that has unproven benefit for patients with iRAP. However, based on predominantly retrospective cohort studies and the notion that pancreas divisum anatomy predisposes some patients to acute pancreatitis, minor papilla endoscopic sphincterotomy (miES) is commonly performed in clinical practice. Although the technique of miES has been performed for >30 years, there has
been only one pilot, open-label, randomized trial of 19 patients with iRAP published over 20 years ago.(Lans, Geenen et al. 1992) This study compared serial dilation of the minor papillary orifice via pancreatic stents - a surrogate for miES - vs. diagnostic ERCP. After mean follow-up of 29-32 months, 6/9 (67%) patients who underwent diagnostic only ERCP developed at least one bout of acute pancreatitis as compared to
1/10 (10%, $p<0.05$) that underwent serial pancreatic duct stent placement. Serial stent placement has been replaced by miES in clinical practice since

serial stenting requires multiple ERCPs and increases the risk of stent-associated main duct strictures.

Several retrospective cohort studies also support the practice of miES for RAP in the setting of pancreas divisum, with >70% of patients in most studies reporting a significant improvement in their disease course (Gerke, Byrne et al. 2004, Attwell, Borak et al. 2006, Chacko, Chen et al. 2008, Borak, Romagnuolo et al. 2009, Crino, Bernardoni et al. 2017). While supporting the role of miES, these studies chose a subjective endpoint (self-perceived improvement) despite their open-label design and absence of a sham comparison group. The controversy is a recurrent topic at national meetings, and opposite positions were nicely summarized after a debate at the 2006 meeting of the American Pancreatic Association (Fogel, Toth et al. 2007). Both sides acknowledged the need for randomized trials, yet there has been little progress in clarifying the benefit of miES on iRAP with pancreas divisum over the past decade.

Study objective

The hypothesis is that obstruction at the level of the minor papilla is one cause of RAP in pancreas divisum; miES will relieve the obstruction, thereby reducing the risk of a recurrent attack(s) of acute pancreatitis.

Study design

This is a sham-controlled, single blinded with a blinded outcome assessment, multi-center, randomized clinical trial of endoscopic retrograde cholangiopancreatography (ERCP) with minor papilla endoscopic sphincterotomy (miES) for the treatment of recurrent acute pancreatitis (RAP) with pancreas divisum. ERCP with miES is often offered in clinical practice to patients with RAP, pancreas divisum, and no other clear risk factors for their acute pancreatitis episodes. The trial requires a total sample size of approximately 234 subjects, and a planned enrollment period of approximately 3.5 years with total planned study duration of 5 years (minimum follow-up of 6 months, maximum follow-up of 48 months).

Intervention

Sham Comparator: EUS + Sham
Experimental: EUS + ERCP with miES

Study burden and risks

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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.Patient must consent to be in the study and must have signed and dated an approved consent form.
2.>18 years
3.Two or more episodes of acute pancreatitis, with each episode meeting two of the following three criteria:
*abdominal pain consistent with acute pancreatitis (acute onset of a persistent, severe, epigastric pain often radiating to the back)
*serum lipase activity (or amylase activity) at least three times greater than the upper limit of normal
*characteristic findings of acute pancreatitis on CECT, MRI or transabdominal ultrasonography4.At least one episode of acute pancreatitis within 24 months of enrollment

5.Pancreas divisum confirmed by prior MRCP that is reviewed by an abdominal radiologist at the recruiting site.
6.By physician assessment, there is no certain explanation for recurrent acute pancreatitis.
7.Subjects must be able to fully understand and participate in all aspects of the study, including completion of questionnaires and telephone interviews, in the opinion of the clinical investigator
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Exclusion criteria

Exclusion Criteria:
1.Prior minor papilla therapy (endoscopic or surgical)
2.Calcific chronic pancreatitis, defined as parenchymal or ductal calcifications identified on computed tomography or magnetic resonance imaging scan that is reviewed by an expert radiologist at the recruiting site.
3.Main pancreatic duct stricture*
4.Presence of a structural etiology for acute pancreatitis, such as anomalous pancreatobiliary union, periampullary mass, or pancreatic mass lesion on imaging*
5.Presence of a local complication from acute pancreatitis which requires pancreatogram
6.Regular use of opioid medication for abdominal pain for the past three months
7.Medication as the etiology for acute pancreatitis by physician assessment
8.TWEAK score >= 4

Study design

Design

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

Recruitment

NL

Recruitment status:	Pending
Start date (anticipated):	25-02-2019
Enrollment:	10
Type:	Anticipated

Ethics review

Approved WMO

Date:	13-01-2020
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)

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
ClinicalTrials.gov	NCT03609944
CCMO	NL68829.091.19