# Preventing recurrent *idiopathic* acute pancreatitis through laparoscopic cholecystectomy (PICUS-2): a multicenter randomized trial

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| **Ethical review** | Approved WMO |
| **Status** | Recruiting |
| **Health condition type** | Gastrointestinal inflammatory conditions |
| **Study type** | Interventional |

## Summary

### ID

NL-OMON53591

**Source**
ToetsingOnline

**Brief title**
PICUS-2

### Condition

- Gastrointestinal inflammatory conditions
- Gastrointestinal therapeutic procedures

**Synonym**
idiopathic pancreatitis, inflammation of the pancreas with an unknown origin

**Research involving**
Human

## Sponsors and support

**Primary sponsor:** Amsterdam UMC
**Source(s) of monetary or material Support:** ZonMw

## Intervention

**Keyword:** Cholecystectomy, Efficacy, Idiopathic acute pancreatitis, Surgery

## Outcome measures

### Primary outcome

The primary outcome measure for this trial is a confirmed recurrent acute pancreatitis (irrespective of the aetiology of recurrent pancreatitis) within one year from the date of randomization

### Secondary outcome

The secondary outcome measures for this trial are

- Readmission for one or more of the following reasons: Recurrent pancreatitis; Cholecystitis; Cholangitis; Obstructive choledocholithiasis needing endoscopic retrograde cholangiopancreatography; Gallstone colic.

- Complications of LC: Bile duct injury and bleeding; Requiring the need for additional surgical endoscopic, or radiological intervention; infection; Other complications such as pneumonia, bacteremia, and new-onset organ failure.

- Number and severity of recurrent episodes of pancreatitis

- Quality of life (QALY)

- Costs (hospital and societal)

- Cost-effectiveness

# Study description

### Background summary

Acute pancreatitis occurs in 6,500 patients annually in the Netherlands. In 25% of these cases no definitive cause can be determined after routine medical check-up. These cases are deemed to be idiopathic acute pancreatitis (IAP). IAP has a high recurrence rate due to the unknown cause of the disease. It is hypothesized that microlithiasis and biliary sludge are the most common causes of IAP. Laparoscopic cholecystectomy (LC) is highly effective in treating microlithiasis and biliary sludge as a cause of acute pancreatitis. Currently no trial has been done comparing LC with conventional treatment for IAP in patients with *true* idiopathic acute pancreatitis, where an EUS (endoscopic ultrasound) has been performed.

### Study objective

The goal of this trial is to determine the efficacy of LC in patients with IAP in the prevention of recurrent acute pancreatitis and biliary events. The secondary goal of this trial is to assess the occurrence of biliary events, complications of LC, number and severity of recurrent episodes of pancreatitis, quality of life (QALY), costs (hospital and societal) and cost-effectiveness.

Only *true* idiopathic acute pancreatitis will be included, excluding all patients with biliary acute pancreatitis. To accomplish this goal EUS will be performed in all included patient and solely EUS negative patients will be included.

### Study design

This study was designed to be a multicenter randomized controlled superiority trial. Patients with a first episode of idiopathic will be screened for eligibility. These patients have undergone the routine work-up for acute pancreatitis as described in appendix A. In this work-up an EUS after repeat transabdominal ultrasound will also be performed. When this work-up does not reveal a definitive aetiology of the acute pancreatitis, idiopathic acute pancreatitis as a diagnosis is assumed. Informed consent to participate in the PICUS-2 trial will be obtained from these patients. In total 262 patients will

be included in this trial. Patients will be randomized in two groups. Patients in one group will receive conventional treatment for idiopathic acute pancreatitis, while the other group receives laparoscopic cholecystectomy. Follow-up will start after the randomization of the patients and will take up one year.

Laparoscopic cholecystectomy will be performed by a surgeon in routine practice. The GI-surgeon will report possible complications of LC, such as bile duct injury and bleeding, requiring the need for additional surgical, endoscopic, or radiological intervention, infection and other complications such as pneumonia, bacteraemia, and new-onset organ failure.

Conventional treatment for idiopathic acute pancreatitis consists of fluid resuscitation, pain treatment and no oral intake (in case of severe pancreatitis). Possible complications following acute pancreatitis must be conservatively treated. If indications for intensive care treatment are present (eg. Shock or respiratory insufficiency) intensive care treatment will be initiated.

Should the patient be readmitted for a recurrence of acute pancreatitis after the routine work-up could not find a cause for this recurrent episode, performing an additional MRCP is recommended in order to rule out structural anomalies such as pancreas divisum, as is in accordance with current guidelines.

All included patients will be asked to fill out five questionnaires over a period of 12 months. The questionnaire contains questions concerning the quality of life of the patient in a validated Dutch translation. The patient will also be asked to grant permission to the investigators regarding access to their medical records to collect data on medical history, readmissions, recurrence and complications.

### Intervention

The intervention of this study is a laparoscopic cholecystectomy performed within four weeks of the first episode of idiopathic acute pancreatitis or during initial admission.

### Study burden and risks

The risks of a cholecystectomy are small and include a 0.5% risk of bile duct injury and 5% risk of (wound) infection. A further burden for the patient is the recovery period ranging from one to max four weeks until full recovery.

As a result of this study it is expected/ estimated that a relative reduction of 60% of recurrent pancreatitis can be achieved by performing laparoscopic cholecystectomy. Pancreatitis causes severe pain to the patient in combination

with a 3 to 5% risk of mortality, therefore a reduction in recurrent acute pancreatitis cases significantly reduces these burdens for the patient.

## 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 older than 18 years
2. First episode of idiopathic acute pancreatitis
3. Full required diagnostic work-up of patient has been performed, including EUS
4. Informed consent for participation was obtained

### Exclusion criteria

1. Patients with recurrent acute pancreatitis
2. Diagnosis of chronic pancreatitis
3. Patients with a pancreatic malignancy
4. Patients who have received a laparoscopic cholecystectomy prior to PICUS-2
5. Patients in whom a known etiology is found during diagnostic work-up
6. Patients in whom complete diagnostic work-up by EUS is not possible (eg. Roux-en-y bypass)

## Study design

### Design

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| Study type: | Interventional |
| Intervention model: | Parallel |
| Allocation: | Randomized controlled trial |
| Masking: | Open (masking not used) |

**Primary purpose:** Prevention

### Recruitment

NL

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|---|---|
| Recruitment status: | Recruiting |
| Start date (anticipated): | 19-01-2024 |
| Enrollment: | 220 |
| Type: | Actual |

## Ethics review

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| Approved WMO Date: | 18-07-2023 |
| Application type: | First submission |
| Review commission: | METC Amsterdam UMC |
| Approved WMO Date: | 27-05-2024 |
| Application type: | Amendment |

Review commission: METC Amsterdam UMC

# 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 | NCT06391359 |
| CCMO | NL82531.018.23 |