ISRCTN74448884 https://doi.org/10.1186/ISRCTN74448884

Which is the best endoscopic treatment for achalasia in children?

Submission date 09/02/2022	**Recruitment status** No longer recruiting	[ ] Prospectively registered [ ] Protocol [ ] Statistical analysis plan [ ] Results [ ] Individual participant data [ ] Record updated in last year
Registration date 18/02/2022	**Overall study status** Ongoing	
Last Edited 03/12/2024	**Condition category** Digestive System	

Plain English summary of protocol

Background and study aims
Achalasia of the gullet is a disease that causes difficulties with swallowing. Children can feel pain during swallowing, but the feeling that food gets stuck is the most common. If achalasia progresses, children start to lose weight or stop growing. In children with achalasia, the gullet stops working and the valve between the gullet and the stomach does not open properly. The underlying cause is unknown. Achalasia always needs treatment.
The most common treatments are aimed at disrupting the valve between the gullet and the stomach. A balloon can be inflated within that valve (endoscopic balloon dilation or EBD) or the valve can be cut open during an endoscopic procedure (per-oral endoscopic myotomy or POEM). The aim of this study is to find out which treatment is best for children.

Who can participate?
Children aged 7 up to and including 17 years with achalasia who have never had treatment before

What does the study involve?
Participants are randomly allocated to be treated with EBD or POEM and are asked to fill out questionnaires before and several times after treatment. A year after the first treatment, control tests are performed to check how well the gullet is functioning.

What are the possible benefits and risks of participating?
The benefits include a very thorough follow up. The risks include not being able to choose your own treatment. Both treatment options carry the risk of rupturing the gullet during the procedure and of reflux disease after the procedure. From adult studies, it seems that POEM may be more effective but causes more reflux disease afterwards.

Where is the study run from?
Amsterdam UMC (The Netherlands)

When is the study starting and how long is it expected to run for?
January 2021 to December 2026

Who is funding the study?
Amsterdam UMC (The Netherlands)

Who is the main contact?
Carlijn Mussies / Michiel van Wijk
pedpoem@amsterdamumc.nl)

Contact information

Type(s)
Principal investigator

Contact name
Dr Michiel van Wijk

ORCID ID
https://orcid.org/0000-0002-8112-8414

Contact details
Meibergdreef 9
Amsterdam
Netherlands
1105AZ
+31 (0)205669111
pedpoem@amsterdamumc.nl

Additional identifiers

Protocol serial number
NL68967.018.20

Study information

Scientific Title
Peroral endoscopic myotomy vs endoscopic balloon dilation for the treatment of achalasia in children

Acronym
PEDPOEM

Study objectives
Peroral endoscopic myotomy (POEM) is a more effective first-line treatment for pediatric achalasia as compared to endoscopic balloon dilation (EBD).

Ethics approval required
Old ethics approval format

Ethics approval(s)

Approved 21/06/2021, Medical Ethical Committee Amsterdam UMC (Trinitygebouw C, room 148 (secretariat), Pietersbergweg 17, 1105BM Amsterdam, The Netherlands; Tel: not available; mecamc@amsterdamumc.nl), ref: 2021_028#B2021374

Primary study design
Interventional

Study design
Randomized non-blinded interventional trial

Study type(s)
Treatment

Health condition(s) or problem(s) studied
Achalasia

Interventions
Endoscopic balloon dilation:
In this study EBD will be performed by experienced (pediatric) gastroenterologists that have independently performed at least 15 procedures. The procedure will be recorded on video to make evaluation afterwards possible. Pictures to evaluate the LA grade of gastroesophageal reflux disease (GERD) will be taken. Patients will be treated under general anesthesia with endotracheal intubation. Patients are asked to use a diet with fluids starting at least 48 hours before the procedure, only clear fluids starting 24 hours and nil per mouth starting 8 hours before the procedure. Initial EBD treatment will consist of a series of two dilatation sessions, scheduled 2 weeks (10-18 days) apart. In the first session, two dilations of 1 minute each with a dilatation pressure of respectively 5 and 8 psi will be performed using a single-use low-compliance 30 mm balloon under radiological guidance. The second treatment session is identical but with a larger balloon with a diameter size of 35 mm. Patients are discharged without any diet restriction. If patients in the EBD treatment arm have symptom recurrence and fulfill the criteria for treatment failure within 6 months after their first dilation, a subsequent dilation with a 35-mm balloon is performed and considered part of the initial EBD treatment. If symptom recurrence occurs after 6 months of initial treatment, this is considered as ‘treatment failure’. Relapse therapy will then be offered at the discretion of the local preferences of the attending physician.

Per-oral endoscopic myotomy (POEM):
POEM will be performed by experienced (pediatric) endoscopists, who have independently performed over 15 procedures. Patients are admitted 2 hours prior to the POEM procedure and are scheduled to be discharged within 48 hours post-procedure. Patients are asked to use a diet with clear fluids starting 48 hours before the procedure and nil per mouth starting 8 hours before the procedure. On the day of the procedure, antibiotics and double dose PPI are administered intravenously. The mouth, throat and esophagus are rinsed with saline and chlorhexidine (40–60 ml). POEM procedures are then performed as described by Inoue et al. The endoscopic procedure will be recorded on video to make evaluation afterwards possible. Pictures to evaluate the LA grade of GERD will be taken. A forward-viewing upper endoscope is used with a transparent distal cap. Carbon dioxide gas is used for insufflation during the procedures. An endoscopic dissection knife is used to access the submucosa, to create the submucosal tunnel, and also to divide circular muscle fibers over a minimum length of 6 cm in the esophagus, and 2 cm onto the cardia according to the standards of surgical myotomy. An

electrogenerator is used with Endocut Q mode (effect 2) to open the mucosa, and spray coagulation mode (effect 2, 50 watts) to dissect the submucosa and divide the muscle fibers. A coagulating forceps is used for hemostasis as needed. Closure of the mucosal entry site is performed using standard endoscopic clips. On the next day postoperative fluoroscopy is performed to rule out a leak at the esophageal closure site before discharge. Patients are kept nil per mouth until after the fluoroscopy and are kept on a liquid diet for an additional 24 h. Patients are discharged with a soft diet for 2 weeks.

Randomisation process:
Randomization will be performed by using a web-based program (Castor electronic data capture (EDC) system) and will be stratified per center, to reach equal number of patients treated with POEM or EBD in each center. To ensure balance of treatment groups with respect to prognosis per subtype and experience in POEM and EBD per center, stratified block randomization with randomly selected block sizes in order to minimize selection bias will additionally be performed within each center. Castor EDC will generate the allocation sequence.

Intervention Type
Procedure/Surgery

Primary outcome(s)
The need for any retreatment (also including retreatment that is planned before 12 months follow-up, but scheduled after 12 months follow-up), as suggested by the treating physician, using Eckhardt score, high-resolution manometry (HRM), and barium esophagram at 3, 6 and 12 months follow-up or during clinically indicated emergency interim visits. The indication for re-treatment is to be confirmed by a majority of three researchers who are blinded to the treatment arm of the patient. In case a patient does not adhere to the protocol, or is lost to follow-up, available data from the last included timepoint are used for estimation of the primary endpoint in an intention to treat analysis.

Key secondary outcome(s)
1. Achalasia symptoms defined by the Eckardt symptom score at 3, 6 and 12 months
2. Health-related and disease-specific quality of life (QoL) measured using the Pediatric Quality of Life inventory (PedsQL + PEDSQL-GI) and achalasia disease-specific QoL questionnaire (DSQoL) at 3, 6 and 12 months
3. Gastroesophageal reflux disease (GERD) symptoms defined by the reflux disease questionnaire (RDQ) at 3, 6 and 12 months
4. Grade of esophagitis defined by Los Angeles (LA) grade during esophagogastroduodenoscopy (EGD) at 12 months
5. Degree of GERD defined by 24-hour pH-impedance (pH-MII) measurement parameters at 12 months
6. Esophageal and lower esophageal sphincter function defined by high-resolution manometry (HRM) parameters at 12 months
7. Procedure-related complications (any unwanted events that arise following treatment and/or that are secondary to the treatment) measured using clinical symptoms and/or observation and appropriate additional testing at 3, 6 and 12 months
7.1. Severe: resulting in admission >24 hours or prolongation of an already planned admission of >24 hours, admission to a medium or intensive care unit, additional endoscopic procedures, blood transfusion or death
7.2. Mild: all other complications
8. Procedure times measured using a digital timer at baseline intervention(s) and during the retreatment procedure

9. Growth (absolute growth in cm and kg, as well as relative growth measured as the change in SD scores [height for age and weight for height]) measured using the digital scale supplied by the hospital at 1, 2, 3, 4, 5, 6, 7, 8, 9, 10, 11 and 12 months
10. Cost-effectiveness evaluated using the hospital declaration system at 12 months

Completion date
31/12/2026

Eligibility

Key inclusion criteria
1. Eckardt score >3
2. Presence of a HRM pattern consistent with achalasia type I or II according to the Chicago classification (CC) V3.0 criteria
3. Age 7 years up to 17 years inclusive

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Child

Lower age limit
7 Years

Upper age limit
17 Years

Sex
All

Key exclusion criteria
1. Achalasia type III (this extremely rare subtype in children that is accompanied by esophageal spasm and associated complaints has a worse prognosis compared to type I and II. Literature and expert-opinion based recommendations suggest to treat type III with POEM. Randomizing these patients to EBD with a high a priori risk of relapses is therefore considered unethical)
2. Previous surgical or endoscopical achalasia treatment
3. Previous surgery of the upper gastrointestinal tract
4. Known coagulopathy
5. Known Liver cirrhosis and/or esophageal varices
6. Known LA grade ≥B esophagitis
7. Known Barrett’s esophagus
8. Known pregnancy at time of treatment
9. Stricture of the esophagus
10. Known presence of malignant or premalignant esophageal lesions

11. Hiatal hernia >1 cm based on HRM measurement
12. Extensive, tortuous dilatation (>7 cm luminal diameter, S shape) of the esophagus
13. Barium esophagram suggestive of other pathologies

Date of first enrolment
09/02/2022

Date of final enrolment
31/12/2025

Locations

Countries of recruitment
Netherlands

Study participating centre
Amsterdam UMC
Meibergdreef 9
Amsterdam
Netherlands
1105AZ

Sponsor information

Organisation
Amsterdam University Medical Centers

ROR
https://ror.org/05grdyy37

Funder(s)

Funder type
Charity

Funder Name
Stichting steun Emma

Results and Publications

Individual participant data (IPD) sharing plan

The data-sharing plans for the current study are unknown and will be made available at a later date

IPD sharing plan summary

Data sharing statement to be made available at a later date