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Treatment of reflux disease using targeted physiotherapy

Submission date 24/05/2023	**Recruitment status** Recruiting	[X] Prospectively registered [X] Protocol [X] Statistical analysis plan [_] Results [_] Individual participant data [_] Record updated in last year
Registration date 05/06/2023	**Overall study status** Ongoing	
Last Edited 03/09/2025	**Condition category** Digestive System	

Plain English summary of protocol

Background and study aims
Gastro-oesophageal reflux disease (GORD) is a common condition where acid from the stomach leaks up into the oesophagus (gullet). It is a global health issue affecting a significant part of the population, and its incidence is increasing, especially in younger patients. There are many risk factors involved in GERD but most are closely related to lifestyle. The anti-reflux barrier is comprised of many defence mechanisms at the level of the esophagus and stomach, however, the junction of the esophagus and stomach (the esophagogastric junction [EGJ]) and adequate esophageal motility (contractions) play a crucial role in the prevention of pathological reflux and its excessive exposure to the esophageal mucosa (inner lining). The degree of their dysfunction is directly related to reflux severity. The EGJ consists of the lower esophageal sphincter (LES) and the diaphragm, its crural part (CD), respectively. Their tight connection and proper function prevent the return of gastric contents to the esophagus. The diaphragm as a skeletal muscle is partially under voluntary control and its activity and strength can be increased by respiratory physiotherapy. Diaphragmatic breathing training can not only improve EGJ function but also increase the strength of esophageal contraction. Moreover, a complex physiotherapeutic approach also has a positive impact on other important mechanisms of reflux symptoms such as esophageal hypersensitivity. The main aim of this study is to support the evidence for the involvement of physiotherapy as a part of a comprehensive therapeutic approach in patients with GERD.

Who can participate?
Patients over 18 years of age with gastroesophageal reflux disease and persistent reflux symptoms despite lifestyle modification and medical therapy or patients who cannot discontinue antireflux medication due to early return of their symptoms.

What does the study involve?
Participants will complete an initial questionnaire assessing the severity of GERD and the impact of reflux disease on their quality of life, as well as an assessment of current proton pump inhibitor (PPI) medication consumption. They will then come off medication for at least 14 days and undergo an initial gastroscopic examination with biopsy (samples) taken from the lower and middle esophagus to assess the findings in the esophagus (to rule out possible florid inflammation or complication of GERD) and to evaluate microscopic signs of reflux disease.

This will be followed by a 3-month control phase of the study, when patients will keep dietary and regimen measures and use their antireflux medication without changing the dose or type of medication. Their exercise regimen will be the same as they have had long term. At the end of the control phase, they will complete questionnaires.
This is followed by 3 months of the active phase of the study, when patients start training and practicing diaphragmatic breathing using dynamic neuromuscular stabilization (DNS) techniques. At the start patients undergo initial functional esophageal testing after discontinuing of their medication for at least 14 days.
The diaphragmatic breathing training will be led by a specialized physiotherapist. There will be a total of six sessions at 1-week intervals, each session will last 60 minutes and include 30 minutes of soft techniques (including visceral manipulation) + 30 minutes of diaphragmatic breathing training using DNS techniques. Besides these six sessions with the physiotherapist, the patient will practice diaphragmatic breathing training daily for the whole active phase. The patient will also continue to adhere to diet and regime measures and take their antireflux medication with no change in the dose and type of medication. At the end of the active phase, they will complete questionnaires and undergo follow-up examinations.
After the active phase, the follow-up phase will continue for 9 months, where the patients continue to perform regular diaphragmatic breathing training according to the recommended protocol and try to begin to reduce the PPI dose to the dose that still controls their symptoms. In this follow-up phase, there will be two check-ups, where the patients will complete questionnaires and assess their current PPI consumption. A 30-minute check-up by a physiotherapist will also take place at each of these follow-ups to assess the accuracy of diaphragmatic breathing training.
The final evaluation is at month 15. Patients will first assess their current PPI consumption, and complete the final questionnaires. After stopping PPI treatment they will undergo a final gastroscopic examination with an esophageal biopsy and a set of functional oesophageal examinations. This concludes the study for the patient.

What are the possible benefits and risks of participating?
The risks to the patients from this study are minimal. They will undergo several invasive examinations during the study. The overall risk resulting from the most invasive of the procedures is 0.11% (such as bleeding). The questionnaire always takes at most 5 minutes to complete.

Where is the study run from?
Pilsen University Hospital and Pavel Kolář´s Centre of Physical Medicine (Czech Republic)

When is the study starting and how long is it expected to run for?
October 2022 to December 2027

Who is funding the study?
Charles University (Czech Republic)

Who is the main contact?
Dr Lucie Zdrhová, zdrhoval@fnplzen.cz

Contact information

Type(s)
Scientific

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Additional identifiers

Study information

Scientific Title
Short-term and long-term effect of diaphragmatic breathing training on reflux symptoms, quality of life, proton pump inhibitor consumption and severity of reflux exposure in patients with gastroesophageal reflux disease unresponsive to conservative management: a prospective, self-controlled bicentric study

Study objectives
Main study hypothesis:
1. Diaphragmatic breathing training improves the antireflux barrier function and thus relieves reflux symptoms and improves quality of life in patients with gastrooesophageal reflux disease

Side study hypotheses:
2. Regular practice of diaphragmatic breathing training allows reduction of proton pump inhibitors consumption in patients with gastroesophageal reflux disease
3. Regular practice of diaphragmatic breathing training results in reduced exposure of the esophageal mucosa to gastric contents
4. Diaphragmatic breathing training leads to optimized lower esophageal sphincter function assessed by high-resolution manometry

Ethics approval required
Old ethics approval format

Ethics approval(s)
1. Approved 03/11/2022, Ethical committee University Hospital Pilsen and Faculty of Medicine in Pilsen Charles University (Edvarda Benese 1128/13, 305 99 Pilsen, Czech Republic; +420 (0)377 402 239; etickakomise@fnplzen.cz), ref: 450/22
2. Approved 09/11/2022, Ethics Committee of IKEM and Thomayer Hospital in Prague (Thomayer Hospital, Videnska 800, 140 59, Prague 4, Czech Republic; +420 (0)261 083 481; eticka.

komise@ftn.cz), ref: 29719/22; G-22-44
3. Approved 30/11/2022, Ethics Committee for Multicenter Clinical Trials of the University Hospital Motol and 2nd Faculty of Medicine, Charles University in Prague (V Úvalu 84, 150 06, Prague 5, Czech Republic; +420 (0)224 431 195, etickakomise@fnmotol.cz), ref: EK – 1379/22

Primary study design
Interventional

Study design
Prospective interventional bicentric self-controlled unblinded trial

Study type(s)
Quality of life, Treatment, Efficacy

Health condition(s) or problem(s) studied
Gastroesophageal reflux disease with refractory symptoms despite proton pump inhibitor therapy or an inability to discontinue medical treatment due to early recurrence of symptoms

Interventions
The study is unblinded, the patients are self-controlled, and the intervention involves physiotherapy performed by a specialist physiotherapist and consists mainly of visceral manipulation techniques and diaphragmatic breathing training using Dynamic Neuromuscular Stabilization (DNS) techniques. For each patient enrolled in the study the researchers will compare two consecutive periods - the first without intervention (i.e. 3 months of a conservative approach with dietary measures and standard antireflux medication) with a subsequent intervention period (i.e. 3 months of physiotherapy performed by a specialist physiotherapist comprising visceral manipulation techniques and training with daily practice of diaphragmatic breathing using DNS techniques). The follow-up will last for the next 9 months, when patients continue the daily practice of diaphragmatic breathing training.

Intervention Type
Procedure/Surgery

Primary outcome(s)
Reflux symptoms and quality of life in GERD patients after 3 months of diaphragmatic breathing training are measured using a Gastroesophageal Reflux Disease Questionnaire (GerdQ) and GERD – Health Related Quality of Life (GERD-HRQL) questionnaire. The questionnaires are assessed at baseline, 3, 6, 9, 12 and 15 months

Key secondary outcome(s)
1. Proton pump inhibitor consumption after diaphragmatic breathing training, measured in mg per week at baseline, 9, 12 and 15 weeks:
1.1. Omeprazole dose – mg/week
1.2. Pantoprazole dose – mg/week
1.3. Esomeprazole dose – mg/week
1.4. Lansoprazole dose – mg/week
1.5. Rabeprazole dose – mg/week

2. Antireflux barrier function after diaphragmatic breathing training, evaluated by high-resolution manometry and 24-hour esophageal pH monitoring with impedance at 3, 6 and 15 months

3. Variables overview evaluated according to the latest version of Chicago classification 4.0:
3.1. Mean LES pressure, mmHg
3.2. IRP (integrated relaxation pressure), mmHg
3.3. EGJ type – EGJ I – III (a, b)
3.4. DCI (distal contractile integral), mmHg.cm.s
3.5. Ineffective esophageal motility, %
3.6. EGJ-CI (EGJ – contractile integral), mmHg.cm
3.7. Mean intragastric pressure, mmHg
3.8. LES function optimization – improvement in mean LES pressure and/or IRP and/or EGJ-CI, yes /no
3.9. AET (acid exposure time), %
3.10. Total number of reflux episodes on impedance/24 h
3.11. SI (symptom index), %
3.12. SAP (symptom association probability), %
3.13. MNBI (mean nocturnal baseline impedance), Ohm
3.14. Proximal reflux episodes (15 cm above LES), %

Other variables overview:
4. Demographic parameters assessed as standard at baseline, 3, 6 and 15 months:
4.1. Age, years
4.2. Sex, male/female
4.3. BMI, kg/m²

5. Macroscopic changes on esophagogastroduodenoscopy (EGDS) evaluated according to the Los Angeles classification (LA A-D) at baseline, 6 and 15 months
6. Microscopic reflux changes of esophageal mucosa evaluated according to Esohisto project 2010, score 0-12 points at baseline, 6 and 15 months
7. Abdominal cavity expansiveness (intraabdominal pressure) evaluated using the DNS brase instrument based on the publication by Jakub Novak at 3 and 6 months

Completion date
31/12/2027

Eligibility

Key inclusion criteria
1. Patients with GERD with persistent symptoms despite lifestyle modification and maintenance therapy with proton pump inhibitors, or patients who cannot discontinue antireflux medication due to early recurrence of their symptoms.
GERD is diagnosed by positive EGDS and/or positive 24-hour esophageal pH monitoring with impedance and symptoms of GERD are present for at least 6 months prior to diagnosis.
1.1. Positive EGDS = evidence of reflux esophagitis according to the Los Angeles classification
1.2. Positive 24-hour esophageal pH monitoring with impedance = AET > 6% and/or number of reflux episodes >80/24 h performed without antireflux medication (off proton pump inhibitor [PPI] 14 days prior to testing)
2. Patients with GERD who are interested in incorporating diaphragmatic breathing training into their treatment
3. PPI dosing on a long-term on-demand basis or regular basis, in either a standard dose (once

daily) or full dose (twice daily).
4. Age 18 years and above
5. Signed informed consent

Participant type(s)
Patient

Healthy volunteers allowed
No

Age group
Adult

Lower age limit
18 Years

Upper age limit
65 Years

Sex
All

Key exclusion criteria
1. Severe reflux esophagitis, i.e. reflux esophagitis LA C and D, esophageal stenosis undergoing dilatation therapy, esophageal varices
2. Other primary esophageal diseases such as achalasia, esophageal tumors
3. Behavioural oesophageal disorders such as rumination and supragastric belching
4. Large hiatal hernia, i.e. manometric EGJ type III with LES-CD separation ≥3 cm
5. Severe comorbidities (diabetes mellitus with organ complications, advanced organ failure, i.e. chronic heart failure, severe COPD, severe renal or hepatic dysfunction, scleroderma or other connective tissue disease, mental disorders, neuropathy)
6. Other GIT disorders requiring regular antisecretory medication that do not allow discontinuation (e.g., Barrett's esophagus, gastroduodenal ulcer disease)
7. Pregnancy, lactation
8. Morbid obesity with BMI above 35 kg/m²
9. Severe musculoskeletal conditions or disorders not allowing training and practice of diaphragmatic breathing (e.g. conditions following spinal surgery)
10. Inability to undergo EGDS, HRM and 24-hour esophageal pH monitoring with impedance (e.g. conditions following nasal surgery with inability to insert transnasal probes)

Date of first enrolment
01/07/2023

Date of final enrolment
01/07/2027

Locations

Countries of recruitment
Czech Republic

Study participating centre
Pilsen University Hospital
I. Department of Internal Medicine, Charles University in Prague, Faculty of Medicine and University Hospital in Pilsen
Alej Svobody 80
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Study participating centre
Pavel Kolář´s Centre of Physical Medicine
Walterovo náměstí 329/2
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Sponsor information

Organisation
Charles University

ROR
https://ror.org/024d6js02

Funder(s)

Funder type
University/education

Funder Name
Charles University, programme Cooperatio

Results and Publications

Individual participant data (IPD) sharing plan
Data will be available for meta-analysis or systematic review upon request from the author after the study is published (Lucie Zdrhová, zdrhoval@fnplzen.cz). The statistically processed anonymised data will be available after the publication of the study for 10 years for meta-

analysis or systematic review purposes. The raw data will be shared for the same period upon relevant request. The anonymisation of data and participants' consent to data processing is addressed in the patient's informed consent for the study.

IPD sharing plan summary

Available on request

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Participant information sheet			30/05/2023	No	Yes
Protocol file			13/07/2023	No	No
Statistical Analysis Plan			13/07/2023	No	No