

Exercise training in Diastolic Heart Failure

Submission date 23/08/2011	Recruitment status No longer recruiting	<input checked="" type="checkbox"/> Prospectively registered <input checked="" type="checkbox"/> Protocol
Registration date 06/10/2011	Overall study status Completed	<input type="checkbox"/> Statistical analysis plan <input checked="" type="checkbox"/> Results
Last Edited 15/08/2025	Condition category Circulatory System	<input type="checkbox"/> Individual participant data

Plain English summary of protocol

Background and study aims

Heart failure with preserved ejection fraction (HFpEF) is one of the three main types of heart failure. It is a common disease, especially in the elderly. Typical risk factors are high blood pressure (hypertension), diabetes, and an inappropriate lifestyle. The consequences are substantial functional limitations and poor quality of life. Patients are also less able to exercise and this has a negative effect on the disease. Currently there is currently no effective treatment but exercise training may be of potential benefit. In this study we want to find out whether regular supervised exercise training can improve patients symptoms, their quality of life and the course of the disease.

Who can participate?

To take part you need to be aged 18 years old or above and have been diagnosed with HFpEF.

What does the study involve?

You will receive either individually prescribed supervised exercise training on top of usual care or usual care alone. Usual care involves normal and established control of risk factors such as hypertension or high blood cholesterol levels (hyperlipidemia) for 12 months. The allocation to training or usual care will be by chance. Only one half of the patients will receive exercise training. During the 1-year follow-up period, there will be 5 visits (including blood samples, exercise testing and echocardiography).

What are the possible benefits and risks of participating?

Supervised individually tailored exercise training in stable heart failure patients appears to be a safe treatment, even in elderly patients. In an initial study patients with the same disease were included and there were no adverse events. Exercise may trigger myocardial ischemia (decreased blood flow to the heart) or arrhythmias (irregular heart beat), exercise-related cardiac decompensation (failure of the heart to maintain adequate blood circulation) and inappropriate blood pressure increases. We will minimise these risks by implementation of strict inclusion/exclusion criteria for participants (e.g., blood pressure control, no symptomatic coronary artery disease, inclusion of compensated patients only) and careful evaluation before participation in the study.

In addition, you will undergo an exercise stress test (spiroergometry) and echocardiography before inclusion, and if we expect any exercise-related unfavourable side effects, you will not be included in the study. Your training intensity will be individually adjusted on the basis of pre-

specified criteria (e.g., heart rate). This will be re-evaluated every 3 months, and individual adaptations of training intensity will be performed, if needed. This procedure ensures that training intensity is always under medical control. Exercise training will be supervised by trained supervisors (e.g., physiotherapists).

With the use of safety measures such as permanent supervision and very regular visits, we expect few adverse events.. On the other hand, we do expect significant beneficial effects. The clinical benefit is expected to largely outweigh potential reversible and non-life-threatening side effects.

Where is the study run from?

The study will be performed in Germany and Austria (20 trial sites).

When is study starting and how long is it expected to run for?

Patients will be enrolled in the study between September 2011 and September 2013. Follow-up examinations will continue until October 2014.

Who is funding the study?

The study is funded by the German Research Foundation (Germany).

Who is the main contact?

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Contact information

Type(s)

Scientific

Contact name

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Additional identifiers

Protocol serial number

Version 1.0 valid from 04.08.2011 (22/8/11)

Study information

Scientific Title

Exercise training in Diastolic Heart Failure: A prospective, randomized, controlled study to determine the effects of exercise training in patients with heart failure and preserved ejection fraction

Acronym

Ex-DHF

Study objectives

To determine whether exercise training on top of usual care is superior to usual care alone in improving a clinical composite outcome score including all cause mortality, cardiovascular hospitalisations, symptoms, global self-assessment, exercise capacity and diastolic function in patients with heart failure with preserved ejection fraction.

This is the resulting randomised trial from the pilot study registered under ISRCTN42524037.

Ethics approval required

Old ethics approval format

Ethics approval(s)

Ethics Committee University of Göttingen, Germany and all responsible local (trial sites) ethics committees approved on 5th September 2011

Study design

Multicenter prospective parallel-group randomized controlled trial

Primary study design

Interventional

Study type(s)

Treatment

Health condition(s) or problem(s) studied

Heart failure with preserved ejection fraction (HFpEF, i.e. diastolic heart failure)

Interventions

Experimental intervention: individually prescribed, supervised, combined endurance / strength training for 12 months ($\geq 3x/$ week)

Control intervention: usual care

Intervention Type

Other

Phase

Not Applicable

Primary outcome(s)

Combined outcome score (modified Packer score, Packer et al., 2001). This combined score classifies patients as: 1 (worsened), 0 (unchanged) or +1 (improved).

Key secondary outcome(s)

1. Components of the primary endpoint (all cause mortality, cardiovascular hospitalisations, change in NYHA-Class, change in global self-assessment, change in peak VO₂, change in E/e')
2. Change in echocardiographic parameters of diastolic function [LAVI, Grad of diastolic function, E/e', e', ratio between early (E) and late (atrial - A) ventricular filling velocity (E/A), deceleration time (DT), isovolumic relaxation time (IVRT)], systolic function (LVEF), left ventricular dimensions (LVEDD, LVESD) and structure (LVMI) after 6 and 12 months
3. Change in quality of life (SF-36, MLWHFQ, HADS) after 6 and 12 months
4. Change in ventilatory efficacy (VE/VCO₂) and sub-maximal exercise capacity (anaerobic threshold, 6-min walk distance) after 6 and 12 months
5. Change in neurohumoral activation (NT-proBNP) after 6 and 12 months
6. Safety and tolerability of training intervention
7. Gender aspects of all primary and secondary endpoints

Completion date

31/08/2015

Eligibility

Key inclusion criteria

1. Stable symptomatic heart failure with preserved ejection fraction (diagnosis according to criteria of the European Society of Cardiology: Paulus et al., 2007):
 - 1.1. New York Heart Association (NYHA) II-III, peak VO₂ < 25 ml/kg/min
 - 1.2. Left ventricular ejection fraction (LVEF) ≥ 50%
 - 1.3. Ratio of early transmitral flow velocity (E) to early diastolic mitral annular velocity (E) (E/e') > 15 or (E/e') > 8 < 15
 - 1.4. N-terminal pro-B-type natriuretic peptide (NTproBNP) > 220 ng/L
 - 1.5. Atrial fibrillation
2. Age ≥ 18 years
3. Symptom severity and heart failure medication were stable during the last 4 weeks
4. Written informed consent of the patient

Participant type(s)

Patient

Healthy volunteers allowed

No

Age group

Adult

Lower age limit

18 years

Sex

All

Total final enrolment

322

Key exclusion criteria

1. Non-cardiac causes for heart failure like symptoms:
 - 1.1. Chronic obstructive pulmonary disease (COPD) - Global Initiative for Chronic Obstructive Lung Disease (GOLD) stages \geq II (moderate, severe, very severe)
 - 1.2. Anaemia ($<11\text{mg/dl}$)
 - 1.3. Significant renal dysfunction estimated Glomerular Filtration Rate (eGFR) $< 30\text{ mL/min/1.73m}^2$ body surface area (BSA)
 - 1.4. Significant peripheral artery disease (Fontaine \geq IIb)
 - 1.5. Musculoskeletal disease that contribute to reduced exercise performance
 - 1.6. Specific cardiomyopathy (e.g. amyloidosis etc.)
 - 1.7. Haemodynamically significant valvular disorders
2. Significant coronary artery disease (CAD) [current angina pectoris, Canadian Cardiovascular Society (CCS) \geq II or positive stresstest, myocardial infarction or coronary artery bypass graft within the last 3 months)
3. Any inability or contraindication to participate in ergospirometric testing or in an exercise program (e.g. physiological, mental) or supply essential information (e.g. questionnaire, diary)
4. Ineffective control of resting blood pressure (BP $\geq 140/90\text{mmHg}$ or BP $\geq 160/100\text{mmHg}$ with ≥ 3 antihypertensive drugs) or of resting heart rate (HR $\geq 100\text{bpm}$)
5. Expected low compliance (e.g. by travel distance to trial site; planned absences longer than 4 weeks during follow up) or ongoing drug abuse
6. Concomitant participation in other interventional clinical trials

Date of first enrolment

21/12/2011

Date of final enrolment

31/08/2015

Locations

Countries of recruitment

Austria

Germany

Study participating centre

Department of Cardiology and Pneumology

Göttingen

Germany

37075

Sponsor information

Organisation

Georg-August University of Göttingen (Georg-August-Universität Göttingen) (Germany)

ROR

<https://ror.org/01y9bpm73>

Funder(s)

Funder type

Government

Funder Name

German Research Foundation (DFG) (Germany) (ref: ED 196/2-1, GE 2048/2-1, HA 5812/4-1)

Results and Publications

Individual participant data (IPD) sharing plan

Not provided at time of registration

IPD sharing plan summary

Not provided at time of registration

Study outputs

Output type	Details	Date created	Date added	Peer reviewed?	Patient-facing?
Results article		02/01/2025	07/01/2025	Yes	No
Results article	Secondary analysis of motivation	06/08/2025	15/08/2025	Yes	No
Protocol article	protocol	01/08/2017	12/08/2020	Yes	No