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Exercise training in Diastolic Heart Failure

Submission date 23/08/2011	**Recruitment status** No longer recruiting	[X] Prospectively registered [X] Protocol [_] Statistical analysis plan [X] Results [_] Individual participant data
Registration date 06/10/2011	**Overall study status** Completed	
Last Edited 07/01/2025	**Condition category** Circulatory System	

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

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Additional identifiers

EudraCT/CTIS number

IRAS number

ClinicalTrials.gov number

Secondary identifying numbers

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

Secondary study design
Randomised controlled trial

Study setting(s)
Hospital

Study type(s)
Treatment

Participant information sheet
Not available in web format, please use the contact details to request a patient information sheet

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 (≥3x/ week)

Control intervention: usual care

Intervention Type
Other

Phase
Not Applicable

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

Secondary outcome measures
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

Overall study start date
01/09/2011

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

Age group
Adult

Lower age limit
18 Years

Sex
Both

Target number of participants
320 patients will be recruited and randomised in a 1:1 fashion to training (160 patients) and usual care (160 patients)

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 ≥ II (moderate, severe, very severe)
1.2. Anaemia (<11mg/dl)
1.3. Significant renal dysfunction estimated Glomerular Filtration Rate (eGFR) < 30 mL/min/1.73m^2 body surface area (BSA)
1.4. Significant peripheral artery disease (Fontaine ≥ 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) ≥ 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 >=140/90mmHg or BP >= 160/100mmHg with >= 3 antihypertensive drugs) or of resting heart rate (HR >= 100bpm)
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
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37075

Sponsor information

Organisation
Georg-August University of Gottingen (Georg-August-Unversitat Gottingen) (Germany)

Sponsor details
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Sponsor type
University/education

Website
http://www.uni-goettingen.de/en/sh/1.html

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

Publication and dissemination plan

Not provided at time of registration

Intention to publish date

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?
Protocol article	protocol	01/08/2017	12/08/2020	Yes	No
Results article		02/01/2025	07/01/2025	Yes	No