Train hard is smart for the heart; an exercise study on clinical outcome and mechanisms in heart failure patients

Published: 22-09-2010
Last updated: 03-05-2024

The overall aim of this project is to compare acute and chronic effects of moderate versus high intensity exercise training in HF patients. Specifically, we will:1. Compare the effects of *traditional* moderate intensity versus novel high intensity…

Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Heart failures
Study type	Interventional

Summary

ID

NL-OMON35051

Source
ToetsingOnline

Brief title
HIT-HF

Condition

- Heart failures

Synonym
heartfailure

Research involving
Human

Sponsors and support

Primary sponsor: Universitair Medisch Centrum Sint Radboud
Source(s) of monetary or material Support: Nederlandse Hartstichting

Intervention

Keyword: endothelin, heart failure, high-intensity training, nitric oxide

Outcome measures

Primary outcome

-physical fitness (maximal cycling test)

-NO-mediated endothelial function of the brachial artery (flow-mediated dilation)

-NO-mediated endothelium-dependent and -independent dilation of the forearm resistance arteries

-contribution of endothelin to the baseline forearm resistance artery vascular tone

Secondary outcome

-cardiac function and structure (echocardiography)

-bloodparameters which have a (in)direct relation with the progression and severity of heart failure (e.g. endothelin, cholesterol, LDL, HDL, triglycerides, hs-CRP, fibrinogen, homocysteine, N-terminal pro-brain natriuretic protein)

Study description

Background summary

In Western countries, heart failure (HF) is a major cause of death. Despite current advances in the pharmacological management of HF, the prevalence is rapidly increasing and the prognosis remains poor. Physical fitness is the single best predictor of both cardiac and all-cause deaths among patients with cardiovascular disease and outperforms ejection fraction as a prognostic index (for survival) in HF. Despite the overwhelming evidence to promote physical

activity, little is known regarding the type of exercise that yields optimal beneficial effects in HF. Some studies in healthy subjects or those with cardiovascular risk suggest greater fitness and cardiovascular adaptations after high intensity exercise than with *traditional* moderate exercise. The rationale is that high intensity exercise (i.e. short bouts of exercise at ~90% of the maximal heart rate) allows patients to complete work at higher workload/intensity, but for a short period of time, inducing beneficial peripheral adaptations in vessels and muscles, without overloading the heart. A sound comparison between the effects of *traditional* moderate versus high intensity exercise training in HF patients has never been examined. Peripheral factors, such as endothelial dysfunction and increased vascular tone, are fundamental to the pathogenesis of HF. These peripheral vascular changes can be explained through changes in dilator (i.e. nitric oxide) and constricting (i.e. endothelin-1) pathways. However, the mechanisms responsible for the exercise-related improvement are not fully understood. Reversing the peripheral vascular changes most likely contributes to the positive effects of exercise in heart failure. While evidence supports a role for nitric oxide to partly explain the beneficial effects of *traditional* exercise, no previous study examined the impact of high intensity exercise on nitric oxide in HF. Moreover, the impact of exercise on the vasoconstrictor endothelin-1 in HF patients has never been studied. This is of special interest, as I recently demonstrated a detrimental role of endothelin-1 in explaining the increased vascular tone during physical inactivity and aging.

Study objective

The overall aim of this project is to compare acute and chronic effects of moderate versus high intensity exercise training in HF patients. Specifically, we will:
1. Compare the effects of *traditional* moderate intensity versus novel high intensity exercise training in heart failure patients (NYHA-class II/III). To this end, physical fitness, clinical outcome and cardiovascular function will be examined before and after 12-week of exercise training.
2. Examine the impact of moderate as well as high intensity exercise training in heart failure patients (NYHA-class II/III) on the NO-pathway and ET-pathway. Therefore, I will examine the nitric oxide-mediated endothelial function and endothelin-1-mediated vascular tone before and after the 12-week interventions.

Study design

Randomised intervention study

Intervention

1. moderate-intensity training (traditional training) for 12 weeks (3 times per week)

2. high-intensity training for 12 weeks (3 times per week)
3. control

Study burden and risks

The brachial catheterisation can induce a haematoma (~5%). However, this is completely reversible within 2 weeks and will not lead to permanent damage. Subjects will be informed regarding this potential risk associated with the invasive procedure of the test.

The pharmaceutical drugs are all accepted for human use and will be infused in the forearm only (not in systemic doses), leading to a localised effect only. In addition, all substances will be removed by the body within minutes to hours (dependent on the substance). Moreover, >4,000 studies have previously used one or more of these substances to examine the local effects of endothelin and nitric oxide in the arms or legs of healthy humans as well as various patient groups (including heart failure). To the best of our knowledge, none of these previous studies reported the presence of (serious) adverse events.

Blood will be taken for later analysis. This will be taken from the canula that will be inserted into the brachial artery for the invasive test. Therefore, the number of invasive procedures will be minised to 2.

Exercise training is not assciated with a health risk. Moreover, exercise training typically causes a decreased cardiovascular risk, whilst vascular and cardiac function and structure improve after a period of exercise training. Also a number a previous studies have demonstrated that the cardiac workload during high intensity training is not significantly different to the (traditional)moderate-intensity training. Some studies have even demonstrated that the beneficial effects of exercise on remodelling of the heart are superior during high-intensity training compared with traditional moderate-intensity training in subjects with heart failure. Therefor, both types of exercise are not associated with an increased risk for development of healt-related problems.

Contacts

Public
Universitair Medisch Centrum Sint Radboud

Geert Grooteplein-noord 21
6525 EZ Nijmegen
NL
Scientific

Universitair Medisch Centrum Sint Radboud

Geert Grooteplein-noord 21
6525 EZ Nijmegen
NL

Trial sites

Listed location countries

Netherlands

Eligibility criteria

Age
Adults (18-64 years)
Elderly (65 years and older)

Inclusion criteria

- heart failure class II or III (diagnosed according to the NYHA-classification)
- patients must be in a stable situation (*3 month) using the same medication

Exclusion criteria

- smokers
- diabetes (type I and II)
- mild renal impairment or proteinuria
- hepatic impairment
- hypercholesterolaemia
- exercise-induced ischaemia
- hypertension (grade II; >160 systolic blood pressure or >100 diastolic blood pressure)
- atrial fibrillation
- pre-menopausal females or those on hormone replacement therapy

Study design

Design

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

Primary purpose: Treatment

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	12-07-2011
Enrollment:	90
Type:	Actual

Ethics review

Approved WMO Date:	22-09-2010
Application type:	First submission
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	07-06-2012
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	08-10-2012
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	21-01-2014
Application type:	Amendment
Review commission:	CMO regio Arnhem-Nijmegen (Nijmegen)
Approved WMO Date:	24-06-2014
Application type:	Amendment

Review commission: CMO regio Arnhem-Nijmegen (Nijmegen)

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
CCMO	NL31612.091.10