# Effects of high intensity interval training on skeletal muscle metabolism and oxygenation in patients with chronic heart failure.

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Chronic heart failure (CHF) is a clinical syndrome resulting from a decreased cardiac output, insufficient to maintain adequate tissue oxygenation. As a consequence, CHF patients suffer from fatigue and exercise intolerance. It is widely recognized...

Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Interventie onderzoek

# Samenvatting

## ID

NL-OMON22308

#### Bron

NTR

#### Aandoening

Chronic heart failure, High intensity training, Skeletal muscle metabolism

## Ondersteuning

**Primaire sponsor:** Maxima Medisch Centrum Veldhoven **Overige ondersteuning:** Stichting 'Vrienden van het Hart'

## **Onderzoeksproduct en/of interventie**

### Uitkomstmaten

#### Primaire uitkomstmaten

Changes in skeletal muscle metabolic recovery after submaximal exercise (leg extension in

the supine position) assessed by 31P MR spectroscopy measurements in M. vastus lateralis after 3 months of physical training (rate of post-exercise phosphocreatine increase, expressed as tau-PCr). Changes in skeletal muscle re-oxygenation assessed simultaneously at the same location by Near Infrared Spectroscopy (rate of post-exercise decrease in deoxygenated hemoglobin, expressed as MRT-HHb).

# **Toelichting onderzoek**

#### Achtergrond van het onderzoek

Rationale:

Patients with chronic heart failure (CHF) suffer from exercise intolerance, mainly due to a decreased cardiac output and impaired skeletal muscle function. Exercise training can improve their functional capacity and reduce their symptoms. To date, it remains unclear what the optimal intensity of exercise should be. A recent randomized controlled trail in elderly CHF patients showed a dramatic gain in exercise capacity using high intensity interval training (HIT) as compared to training at a moderate intensity. This study showed improvements in skeletal muscle metabolism, blood flow and cardiac function. However, as all these measurements were performed at rest it is not clear to what extent these changes account for the increase in exercise performance. Yet, such knowledge is necessary for individualized exercise prescription, specifically aimed at the individual patients' limitations. The present study is designed to investigate the effects of HIT on skeletal muscle metabolism (O2 utilization) and oxygenation (O2 delivery) at submaximal exercise.

Objective:

The main objective of the study is to investigate the physiological effects of high intensity interval training (HIT) at the skeletal muscle level by assessing skeletal muscle reoxygenation and skeletal muscle metabolic recovery after submaximal exercise. Secondary objectives are to investigate the effects of HIT on maximal exercise capacity, quality of life and left ventricular function.

Study design:

Prospective randomised controlled intervention trial.

Study population:

Patients with stable systolic CHF (left ventricular ejection fraction < 40%) who are able and motivated to perform an exercise training program.

Intervention:

HIT is performed 3 times a week during 12 weeks and consists of 4 intervals of 4 minutes cycling on a ergometer at 85-95% of the peak aerobic capacity (peak Vo2) separated by 3 minute active pauses at 50-60% of peak Vo2. After each HIT sessions patients will perform muscle resistance training at moderate intensity. The entire program is performed in the hospital under direct supervision of trained physiotherapists.

Main study parameters/endpoints:

Changes in skeletal muscle metabolic recovery after submaximal exercise (leg extension in the supine position) are assessed by 31P MR spectroscopy measurements in M. vastus lateralis (rate of post-exercise phosphocreatine increase, expressed as tau-PCr). Changes in skeletal muscle re-oxygenation are assessed simultaneously at the same location by Near Infrared Spectroscopy (rate of post-exercise decrease in deoxygenated hemoglobin, expressed as MRT-HHb).

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:

No adverse effects of exercise training performed by CHF patients have been reported in literature, nor in our clinical experience. Yet, exercise training was shown to have beneficial effects on maximal exercise capacity, muscle strength and quality of life. The HIT program that will be used in this study has been evaluated extensively in CHF patients and other populations, like elderly patients, and patients with coronary artery disease without any documented harmful effects. In order to reduce potential risks of exercise training, all patients perform a maximal cardiopulmonary exercise test at baseline, excluding patients with myocardial ischaemia and ventricular arrhythmias during exercise. Training sessions will be under supervision of trained physiotherapist in a clinical setting. The assessments that will be done before and after training are completely non-invasive and therefore without additional risks. By performing these measurements, we will be able to evaluate the physiological effects of HIT. This knowledge may eventually be useful for a more individualized exercise prescription, specifically aimed at the patients' individual limitations.

#### Doel van het onderzoek

Chronic heart failure (CHF) is a clinical syndrome resulting from a decreased cardiac output, insufficient to maintain adequate tissue oxygenation. As a consequence, CHF patients suffer

from fatigue and exercise intolerance. It is widely recognized that exercise training can improve functional capacitiy and reduce symptoms in CHF patients. For this reason, exercise training is included in many (inter-)national guidelines for CHF patients. Nevertheless, to date, it still remains unclear what the appropriate or optimal intensity of exercise should be. A recent randomized controlled trail on exercise training in a group of elderly patients with CHF showed a dramatic improvement in exercise capacity using high intensity interval training (HIT) as compared to training at a moderate intensity. Proposed mechanisms for this difference include attained improvement in skeletal muscle metabolism, blood flow and cardiac function. However, the effects of HIT on skeletal muscle metabolism and blood flow have been studied in vitro and in resting conditions only. As such, it is not clear if and to what extent these changes are clinically relevant in terms of exercise intolerance. Moreover, studies on training-induced physiological changes at a muscular level during or directly after exercise in healthy subjects are scarce; in CHF patients such are lacking. Yet, more knowledge on the physiological effects of HIT in CHF patients is important as it will aid clinicians in prescribing this therapy on an individual basis, specifically aimed at the patients' individual limitations.

In order to elucidate the physiological mechanisms underlying the effects of HIT, it is necessary to use established methods for assessing skeletal muscle metabolism (O2 utilization) and muscle tissue oxygenation (O2 delivery) at exercise, preferably simultaneously. As such, skeletal muscle metabolism can be assessed reliably by the rate of post-exercise phosphocreatine (PCr) resynthesis by 31P-MRS (magnetic resonance spectroscopy); exercise-induced changes in muscle tissue oxygenation can be assessed by near-IR spectroscopy (NIRS ). In a recent study we used these methods simultaneously in CHF patients during recovery from submaximal exercise, showing that this approach is feasible in this patient group.

#### Onderzoeksopzet

All measurements as mentioned above will be performed at baseline and after completion of the 3 month training program.

#### **Onderzoeksproduct en/of interventie**

HIT is performed 3 times a week during 12 weeks and consists of 4 intervals of 4 minutes cycling on a ergometer at 85-95% of the peak aerobic capacity (peak Vo2) separated by 3 minute active pauses at 50-60% of peak Vo2. After each HIT sessions patients will perform muscle resistance training at moderate intensity. The entire program is performed in the hospital under direct supervision of trained physiotherapists.

The control group receives care as usual (including lifestyle advice).

# Contactpersonen

# **Publiek**

Postbus 7777 V. Niemeijer de Run 4600 Veldhoven 5500 MB The Netherlands +31 (0)40 88888200

## Wetenschappelijk

Postbus 7777 V. Niemeijer de Run 4600 Veldhoven 5500 MB The Netherlands +31 (0)40 88888200

# **Deelname eisen**

# Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

1. Written informed consent;

2. Stable systolic heart failure secondary to ischemic or dilated cardiomyopathy New York Heart Association (NYHA) class II or III (without change in class or medication < 3 months prior to inclusion);

3. Left ventricular ejection fraction of  $\leq$  40% (assessed within 3 months before inclusion by echocardiography, MRI or radionuclear measurement).

## Belangrijkste redenen om niet deel te kunnen nemen (Exclusiecriteria)

1. Pacemaker / implantable cardioverter defibrillator (ICD) or other contra indication for magnetic resonance imaging;

2. Claustrophobia;

3. Myocardial infarction or unstable angina less than 3 months prior to inclusion;

- 4. Clinical signs of decompensated heart failure;
- 5. Ventricular tachycardia or ischemia during exercise
- 6. Participation in a training program (> 2/week) in the last year;

7. Intracardiac shunts or congenital heart disease limiting exercise capacity;

8. Orthopaedic, vascular, pulmonary, neuromuscular and other disease limiting exercise capacity.

# Onderzoeksopzet

#### **Opzet**

Туре:	Interventie onderzoek
Onderzoeksmodel:	Parallel
Toewijzing:	Gerandomiseerd
Blindering:	Open / niet geblindeerd
Controle:	Geneesmiddel

#### Deelname

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Nederland	
Status:	Werving gestart
(Verwachte) startdatum:	01-11-2010
Aantal proefpersonen:	40
Туре:	Verwachte startdatum

# **Ethische beoordeling**

Positief advies	
Datum:	16-11-2010
Soort:	Eerste indiening

# **Registraties**

## Opgevolgd door onderstaande (mogelijk meer actuele) registratie

ID: 38340 Bron: ToetsingOnline Titel:

### Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

### In overige registers

Register	ID
NTR-new	NL2487
NTR-old	NTR2604
ССМО	NL33837.015.10
ISRCTN	ISRCTN wordt niet meer aangevraagd.
OMON	NL-OMON38340

# Resultaten

#### Samenvatting resultaten

Kemps HMC, Prompers JJ, Wessels B, de Vries WR, Zonderland ML, Thijssen EJM, et al. Skeletal muscle metabolic recovery following submaximal exercise in chronic heart failure is limited more by O2 delivery than O2 utilization. Clin Sci (Lond) 2010 Feb;118:203-10.