Reproducibility of measurement of skeletal muscle tissue oxygenation in patients with chronic heart failure.

No registrations found.

Ethical review	Positive opinion
Status	Recruiting
Health condition type	-
Study type	Observational non invasive

Summary

ID

NL-OMON19931

Source
Nationaal Trial Register

Brief title
Reproducibility of skeletal muscle TSI in CHF

Health condition

Chronic Heart Failure, Exercise intolerance, Skeletal muscle impairment.
Chronisch hartfalen, inspanningsintolerantie, skeletspierbeperking

Sponsors and support

Primary sponsor: Maxima Medical Center
Source(s) of monetary or material Support: Maxima Medical Center

Intervention

Outcome measures

Primary outcome

Difference (paired T-test when normally distributed) and agreement (intra-class correlation coefficients, limits of agreement and coefficients of variation) of the rate of muscle

deoxygenation at exercise onset between two days (rate of decrease of muscle tissue saturation index expressed as MRT-TSI).

Secondary outcome

Difference (independent T-test when normally distributed) of VO2 kinetics (rate of increase in VO2 after onset of submaximal exercise expressed as ô-VO2) and NIRS kinetics (MRT-TSI) between healthy subjects and CHF patients during the first submaximal exercise test.

Study description

Background summary

Rationale:

Patients with chronic heart failure (CHF) suffer from a decreased cardiac output and impaired skeletal muscle function. Skeletal muscle alterations can ultimately have a predominant role in the pathophysiology of exercise intolerance in CHF. However, research indicates that not all CHF patients are impaired in a similar manner, which might explain the large number of non-responders to various types of treatment. Near Infrared Spectroscopy (NIRS) is a promising non-invasive tool that has the ability to discern between impairments of O2 delivery and O2 utilization at the skeletal muscle level. In order to be able to use NIRS as a routine measurement in a clinical setting the issue of reproducibility needs to be addressed. Additionally, by comparing data from healthy subjects with CHF patients, the understanding of the pathophysiology of heart failure might be improved.

Objective:

The main objective of the study is to investigate the reproducibility of NIRS measurements during submaximal exercise in CHF patients. The secondary objective is to investigate the differences in changes of muscle oxygenation during and after exercise between healthy subjects and CHF patients.

Study design:

Prospective observational study without invasive measurements.

Study population:

Twenty patients with stable systolic CHF (left ventricular ejection fraction ¡Ü 40%) and twenty age- and BMI-matched healthy control subjects who are able and motivated to perform cycling exercise.

Main study parameters/endpoints:

Difference and agreement of the rate of muscle deoxygenation at exercise onset between two days (rate of decrease of muscle tissue saturation index expressed as MRT-TSI).

Secundary study parameters/endpoints: Difference of VO2 kinetics and NIRS kinetics (MRT-TSI) between healthy subjects and CHF patients during the first submaximal exercise test.

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

No adverse effects of submaximal cycling exercise performed by CHF patients or healthy subjects have been reported in literature, nor in our clinical experience. Near infrared spectroscopy is a non-invasive measurement and therefore place no additional burden on the subjects. In order to set intensity for the submaximal exercise test, all subjects perform a maximal cardiopulmonary exercise test at baseline, excluding patients with myocardial ischaemia and ventricular arrhythmias during exercise.

By performing these measurements, we will be able to evaluate the reproducibility of NIRS and pathophysiological mechanisms of slowed VO2 kinetics. This study will provide knowledge on the applicability of NIRS in routine clinical assessment of CHF patients, and eventually, will contribute to a more individualized exercise prescription, specifically aimed at the patients individual limitations.

Study objective

Chronic heart failure (CHF) is a clinical syndrome resulting from a decreased cardiac output, insufficient to maintain adequate tissue oxygenation. Eventually, inadequate tissue oxygenation will lead to pathological alterations, especially at the skeletal muscle level. Several studies indicated that, especially in severe heart failure, skeletal muscle alterations can have a predominant role in the pathophysiology of exercise intolerance.(26, 32) In other words, these patients with severe heart failure appear not to be limited mainly by impaired tissue oxygenation but more so by slowed skeletal muscle metabolism. However, the degree of skeletal muscle impairment shows large inter-individual variation, indicating that certainly not all CHF patients are limited in a similar manner.

The continuing appearance of novel treatment modalities in the field of CHF has beneficial effects on group outcome. However, rising costs and potential adverse effects of these treatments call for a more individualized approach to medical treatment. The ability to

discern different types of limitations and to tailor treatment, like physical training and cardiac resynchronization therapy, has the potential of reducing the large number of non-responders (30-50%) to these interventions. Ideally, to disclose the nature of the limitation, a reliable and preferably non-invasive test should be available to guide the clinician dealing with CHF treatment.

Near Infrared Spectroscopy (NIRS) is a promising tool in exercise physiology, as it has the ability to monitor changes in tissue oxygenation in a totally non-invasive setup. The technique is based on the relative tissue transparency for light in the near-infrared region and on the oxygen-dependent absorption changes of haemoglobin and myoglobin. Changes in concentrations of oxygenated haemoglobin (O2Hb) and deoxygenated haemoglobin (HHb) can be measured, reflecting local O2 delivery relative to O2 utilization. In this way, the speed of adaptation of oxygenation to a certain level of exercise reflects the intrinsic pathophysiology of exercise intolerance, as for instance slow deoxygenation at exercise onset indicates a metabolic limitation (utilization), while fast deoxygenation coincides with a limitation in oxygen delivery.

In order to be able to use NIRS as a routine measurement in a clinical setting, some issues need to be addressed. First, to our knowledge, reproducibility of NIRS measurements during exercise has not yet been evaluated in the CHF population. Furthermore, research on differences in exercise-related changes in muscle oxygenation between CHF patients and healthy subjects is scare. Yet, investigating these differences might contribute to a better understanding of the pathophysiology of heart failure.

Study design

1. (t0) Baseline assessment;

2. (t1=t0 + 2-7days) Submaximal exercise test 1;

3. (t2=t1 + 2-7days) Submaximal exercise test 2.

Intervention

The study is designed as a prospective observational study without invasive measurements. After informed consent is obtained, a baseline assessment will be performed. The first part of this assessment consists of a physical examination, echocardiography and maximal exercise testing with respiratory gas analysis. The second part of the assessment consists two six minute submaximal exercise test with simultaneous near infrared spectroscopy (NIRS) measurements.

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Eligibility criteria

Inclusion criteria

1. Written informed consent;

2. Systolic heart failure secondary to ischemic or dilated cardiomyopathy;

3. New York Heart Association (NYHA) class II or III (without change in class or medication < 3 months prior to inclusion);

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

Exclusion criteria

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

2. Clinical signs of decompensated heart failure;

3. Ventricular tachycardia or ischemia during exercise;

4. Participation in a training program (≥ 2/week) in the last year;

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

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

Study design

Design

Study type:	Observational non invasive
Intervention model:	Parallel
Allocation:	Non controlled trial
Masking:	Open (masking not used)
Control:	N/A , unknown

Recruitment

NL

Recruitment status:	Recruiting
Start date (anticipated):	01-02-2012
Enrollment:	40
Type:	Anticipated

Ethics review

Positive opinion

Date:	15-12-2011
Application type:	First submission

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
NTR-new	NL3049
NTR-old	NTR3197
CCMO	NL38993.015.11
ISRCTN	ISRCTN wordt niet meer aangevraagd.

Study results

Summary results

Kemps HM, Schep G, Zonderland ML, Thijssen EJ, De Vries WR, Wessels B, Doevendans PA, Wijn PF. Are oxygen uptake kinetics in chronic heart failure limited by oxygen delivery or oxygen utilization? International journal of cardiology 142: 138-44, 2010.
Kemps HMC, Prompers JJ, Wessels B, de Vries WR, Zonderland ML, Thijssen EJM, Nicolay K, Schep G, Doevendans AFM. Skeletal muscle metabolic recovery following submaximal exercise in chronic heart failure is limited more by O2 delivery than O2 utilization. Clin.Sci.(Lond) 118: 203-210, 2010.