Effect of Iron Deficiency on skeletal muscle metabolism in HFpEF

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Ethische beoordeling	Positief advies
Status	Werving gestart
Type aandoening	-
Onderzoekstype	Observationeel onderzoek, zonder invasieve metingen

Samenvatting

ID

NL-OMON21811

Bron
Nationaal Trial Register

Verkorte titel
Iron Mucle in HFpEF

Aandoening

Heart failure with preserved ejection fraction and iron deficiency

Ondersteuning

Primaire sponsor: Vifor pharma
Overige ondersteuning: Investigator initiated in collaboration with Vifor pharma

Onderzoeksproduct en/of interventie

Uitkomstmaten

Primaire uitkomstmaten

- Is skeletal muscle metabolism impaired in HFpEF patients with iron deficiency, measured using CMR spectroscopy?

Toelichting onderzoek

Achtergrond van het onderzoek

Rationale:
Diabetes, obesity and hypertension, all highly present comorbidities in HFpEF, seem to drive this disease by inducing low-grade systemic inflammation which in turn induces microvascular dysfunction and activates a cascade of events. Several studies have demonstrated that HFpEF is a systemic disease that affects not only cardiac, but also peripheral muscle energy metabolism. Iron deficiency (ID) could be an important contributor in this pathophysiological process.
Iron deficiency is present in 50% of chronic HF patients. Although HFpEF was not excluded from these cohort studies, it mainly included HF with reduced ejection fraction (HFrEF).
We hypothesize that ID is an important factor in the limitation of exercise capacity in HFpEF. Systemic low-grade inflammation does not only lead to microvascular dysfunction but also to iron deficiency. Iron deficiency has a direct effect on the muscle. Not only on the cardiac muscle but also the skeletal muscle is affected, impairing muscle contraction strength but also energy metabolism. The primary focus of this study will be delivering proof that the alterations in the muscle are more severe in HFpEF patients with ID compared to without ID.

Objective:
To assess if skeletal muscle metabolism is impaired in HFpEF patients with iron deficiency compared to HFpEF patients without iron deficiency

Study design: Cross sectional study

Study population: All patients (>18 yr) with HFpEF

Main study parameters/endpoints:
The main study parameters is PCR recovery time, a measurement of PCR recovery time using MR spectroscopy

Secondary parameters/endpoints are:
- Microvascular function
o Glycocalyx thickness (um)
o Heat induced hyperaemic response (% skin hyperaemic response)
- Exercise tolerance
o 6 minute walk test distance (m)
o maximum exercise capacity (METs on exercise test)

Nature and extent of the burden and risks associated with participation, benefit and group relatedness:
There is a minimal burden associated with participation in this study. Measurements of ID are performed as part of routine examinations in the outpatient clinic.

1. MR spectroscopy is a non-invasive, non-radiation imaging technique. CMR has a low risk of

contrast reaction. To date, MRI investigations have been performed in over 200 million patients. Worldwide and are regarded as extremely safe. MRI is painless and has no known short-term or long-term biological adverse effects. Deaths have only been reported when proper safety precautions were not taken.
Risks: There are very few risks known to be associated with MRI:
Changing radiofrequency pulses may produce heat. This is not known to cause any side effects. Loose metal objects in the patient or in the scanner room may cause damage to the patient. When appropriate precautions are taken, this is rare to occur.

2.Glycocalyx thickness measurement is a non-invasive, endothelial function measurement method. This method has no contra-indications or adverse effects.

3.Heat-induced skin hyperaemic response, is a non-invasive, endothelial function measurement method. This method has no contraindications or adverse effects. The warm electrodes (warmth until 44° C) are not painful and just a slight local warmth can be felt.

Doel van het onderzoek

We hypothesize that ID is an important factor in the limitation of exercise capacity in HFpEF. Systemic low-grade inflammation does not only lead to microvascular dysfunction but also to iron deficiency. Iron deficiency has a direct effect on the muscle. Not only on the cardiac muscle but also the skeletal muscle is affected, impairing muscle contraction strength but also energy metabolism. The primary focus of this study will be delivering proof that the alterations in the muscle are more severe in HFpEF patients with ID compared to without ID.

Objective:
To assess if skeletal muscle metabolism is impaired in HFpEF patients with iron deficiency compared to HFpEF patients without iron deficiency

Onderzoeksopzet

From October 2019 until December 2020: patient inclusion. First trimester 2021 data analysis and prepare publication

Onderzoeksproduct en/of interventie

The main study parameters is PCR recovery time, a measurement of PCR recovery time using MR spectroscopy

Secondary parameters/endpoints are:
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Wetenschappelijk

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Deelname eisen

Belangrijkste voorwaarden om deel te mogen nemen (Inclusiecriteria)

In order to be eligible to participate in this study, a subject must meet all of the following criteria:
Group I HFpEF with iron deficiency
Group II HFpEF without iron deficiency

• HFpEF: according to the ESC guidelines
(1) Signs and/or symptoms of heart failure,
(2) LVEF ≥ 50%,
(3) Elevated levels of natriuretic peptide (NT-proBNP > 125 pg/ml
~ 15 pmol/L)
(4) one of the following additional criteria
a) Relevant structural heart disease; LV hypertrophy, (LVmass index > 95 g/m2 in women, or >115 g/m2 in men) and/or LA enlargement (LA volume index >34 l/m2)
b) Diastolic dysfunction (E/e' ≥ 13, mean e' septal and lateral wall < 9 cm/s)
• Iron deficiency: serum ferritin < 100 µg/L or serum ferritin between 100-299 µg/L in combination with a transferrin saturation < 20%.

Belangrijkste redenen om niet deel te kunnen nemen

(Exclusiecriteria)

A potential subject who meets any of the following criteria will be excluded from participation in this study:
- Reproductive age women
- Any iron supplement (oral, iv) during the last 6 months prior to inclusion
- Any chemotherapy in last year
- Significant peripheral artery disease
- Contraindication for CMR
• ODIN protocol:
• “Uitvoering van MRI onderzoek bij patiënten met een cardiaal implanteerbaar elektronisch device (CIED), waaronder een pacemaker en ICD”
• ODIN protocol:
• “Voorbereiding klinische patiënten voor MRI onderzoek”
• Metallic implant (vascular clip, neuro-stimulator, cochlear implant)
• Pacemaker or implantable cardiac defibrillator(ICD)
• Claustrophobia
- Body weight > 130kg

Onderzoeksopzet

Opzet

Type:	Observationeel onderzoek, zonder invasieve metingen
Onderzoeksmodel:	Anders
Toewijzing:	N.v.t. / één studie arm
Blindering:	Open / niet geblindeerd
Controle:	N.v.t. / onbekend

Deelname

Nederland

Status:	Werving gestart
(Verwachte) startdatum:	01-10-2019
Aantal proefpersonen:	78
Type:	Verwachte startdatum

Voornemen beschikbaar stellen Individuele Patiënten Data (IPD)

Wordt de data na het onderzoek gedeeld: Nee

Ethische beoordeling

Positief advies

Datum:	17-10-2019
Soort:	Eerste indiening

Registraties

Opgevolgd door onderstaande (mogelijk meer actuele) registratie

Geen registraties gevonden.

Andere (mogelijk minder actuele) registraties in dit register

Geen registraties gevonden.

In overige registers

Register	ID
NTR-new	NL8095
Ander register	metc AZM/MUMC : METC181034

Resultaten

Samenvatting resultaten
None