Heart failure with preserved ejection fraction (HFpEF), perfusion and metabolism

Published: 24-11-2016
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Ethical review	Approved WMO
Status	Recruitment stopped
Health condition type	Heart failures
Study type	Observational invasive

Summary

ID

NL-OMON47584

Source
ToetsingOnline

Brief title
Heart failure with preserved ejection fraction, early diagnosis

Condition

- Heart failures

Synonym
analysis of the disease, Heart failure, imaging

Research involving
Human

Sponsors and support

Primary sponsor: Academisch Medisch Centrum
Source(s) of monetary or material Support: Health Foundation Limburg

Intervention

Keyword: CMR, Early diagnosis, HFpEF

Outcome measures

Primary outcome

-Impaired perfusion (assessed using CMR): myocardial perfusion reserve

Secondary outcome

-Impaired peripheral muscle metabolism (assessed using MR spectroscopy):

PCr/ATP ratio

-Endothelial dysfunction (1) glycocalyx thickness (2) Heat-induced hyperaemic

response

-Level of fibrosis: T1 mapping on CMR

-Biomarkers of endothelial dysfunction, oxidative stress, fibrosis and

inflammation

Study description

Background summary

The prevalence of heart failure (HF) continues to rise exponentially worldwide, primarily to be attributed to an increase in HFpEF (Heart Failure with preserved Ejection Fraction). HF can be split evenly into HFpEF, formerly classified as diastolic heart failure, and HFrEF (HF with reduced ejection fraction) formerly classified as systolic heart failure. In the Netherlands, approximately 70.000 patients suffer from HFpEF. HFpEF, is characterized by an increased stiffness of the heart, and is associated with multiple comorbidities, such as diabetes, hypertension and obesity. However, HFpEF is more than just a complication of these comorbidities, and consequently requires more than just treatment of these comorbidities. Typical heart failure medications, proven to be successful in HFrEF, such as ace inhibitors and beta-blockers have failed to improve quality of life or survival in HFpEF patients. Currently, no evidence-based treatment can be offered for HFpEF, resulting in poor quality of life, enormous costs and bad outcome. Therefore, a

better understanding of the underlying pathophysiology is essential in order to find a treatment for these patients.
Low-grade inflammation, caused by multiple comorbidities, is suggested to play a central role in HFpEF. It is thought that low-grade inflammation causes fibrosis as well as endothelial dysfunction, which is known to be present in these patients. Indeed, our previous research demonstrated the inability of HFpEF patients to increase myocardial oxygen delivery during exercise, suggesting impaired microvascular function. We therefore hypothesize that peripheral/ generalized endothelial dysfunction results in coronary microvascular dysfunction, accompanied by impaired myocardial microvascular perfusion and impaired cardiac energy metabolism.

Study objective

The objective is to assess whether myocardial microvascular perfusion and myocardial energy metabolism is impaired in HFpEF patients. Additionally we will evaluate whether endothelial dysfunction is associated with diminished myocardial perfusion (e.g. coronary microvascular dysfunction) and impaired myocardial metabolism. We will assess whether non-invasive CMR techniques are valid compared to the gold-standard biopsy

Study design

This study is a prospective case-control study

Group I: HFpEF patients
Group II: controls

Duration: 2 separate days, no treatment intervention or follow-up.
Setting: MUMC+, outpatient clinic cardiology (day 1), radiology (day 2)

In this case control study patients will be assessed for endothelial function, myocardial perfusion and myocardial metabolism.
Measurements will be performed based on standard study protocols. All diagnostic test are routinely used in clinic, with the exception of the non-invasive glycocalyx measurement. (for details see methods section) The whole measurement programme will take place on three separate days and will last approximately 5 hours (day 1) and 2 hours (day 2)

Overview Diagnostic tests
Day 1 Clinical assessment (standard clinical care)
- Echocardiography
- Holter
- 6MWT
- Lung function test
- Exercise test

- ApneaLink
- QoL questionnaires
- Lab

Day 2 Extra assessment as part of this study:
- CMR
- Glycocalyx measurement
- Biobank (METC 14-4-078)

Day 3 Extra assessment as part of this study:
- 31P-MRS (Skeletal Muscle Phosphorus Magnetic Resonance Spectroscopy)

Study burden and risks

Adenosin stress infusion
The use of adenosine infusion in these patients can be regarded as safe and side effects are transient and generally well tolerated. Effects related to the known pharmacology of adenosine are frequent, but usually harmless, self-limiting and of short duration. Discontinuation of infusion may be necessary if the effect is intolerable. Any side effect is rapidly reversed with termination of adenosine infusion, within seconds.

Gadovist should not be used in patients with severe renal impairment (Glomerular filtration rate (GFR) < 30 ml/min/1.73m2 because there have been reports of nephrogenic systemic fibrosis associated with use of some gadolinium-containing contrast agents in these patients, thus these patients will be excluded from the study).

Heat-induced skin hyperaemic response
A method to measure skin microvascular endothelial function is the heat-induced skin hyperaemic response. After an acclimatization period of 30 minutes, microvascular measurements will be performed. Skin blood flow will be measured with laser Doppler flowmetry before (baseline) and during 25 minutes of local heating to 44° C with the heated LDF-probe.
This high temperature does not cause pain or disconfort.

Contacts

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Trial sites

Listed location countries

Netherlands

Eligibility criteria

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

Inclusion criteria

1. All patients
* Age > 50
* Estimated glomerular filtration reserve (eGFR) >30 ml/min
* Body weight<130kg ;1.1. HFpEF group
*Diagnosis of HFpEF, requires three conditions to be satisfied, as stated in the ESC guidelines:
(1) symptoms or signs of heart failure
(2) normal or only mildly reduced LV ejection fraction in a non-dilated LV (LVEF><= 50%)
(3) relevant structural heart disease (LV hypertrophy/LA enlargement) and/or diastolic dysfunction.
*Current BP < 160/90
*Estimated glomerular filtration reserve (eGFR) >30 ml/min

1.2 Hypertensive control patients;*No coronary artery disease (CAD; coronary stenosis>70% or history of CABG)
*No heart failure
*Estimated glomerular filtration rate (eGFR) > 30 ml/min
*Preserved left ventricular ejection fraction (LVEF) (><= 50%) on echocardiography
*No left ventricular hypertrophy (lateral and septal left ventricular wall <=<10mm)
*No left atrium enlargement
*No diastolic dysfunction type 2 or 3

*Blood pressure >140/90 mmHg or use of anti-hypertensive therapy
*Normal cardiac structure and function on echocardiography

Exclusion criteria

A potential subject who meets any of the following criteria will be excluded from participation in this study:;- Age < 50 years
- Life expectancy of <1 year (malignancy etc.)
- 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 (vascularclip, neuro-stimulator, cochlearimplant)
* Pacemaker or implantable cardiac defibrillator(ICD)
* Claustrophobia
* Persistent or chronic atrial fibrillation
- Contraindication to adenosine:
* High degree atrio-ventricular block (2nd or 3rd degree)
* Severe asthma bronchial
* Chronic obstructive pulmonary disease Gold * III
* Concomitant use of dipyridamole (Persantin)
* Long QT syndrome (congenital)
- Contraindication to gadolinium (Dihydroxy- hydroxymethylpropyl- tetraazacyclododecane-triacetic acid (butrol) - Gadovist ®)
* Severe renal impairment (Glomerular filtration rate (GFR) < 30 ml/min/1.73m2

Study design

Design

Study type:	Observational invasive
Intervention model:	Other
Allocation:	Non-randomized controlled trial
Masking:	Open (masking not used)
Control:	Active
Primary purpose:	Diagnostic

Recruitment

NL

Recruitment status:	Recruitment stopped
Start date (anticipated):	28-06-2017
Enrollment:	40
Type:	Actual

Ethics review

Approved WMO Date:	24-11-2016
Application type:	First submission
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	29-12-2017
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)
Approved WMO Date:	01-05-2019
Application type:	Amendment
Review commission:	METC academisch ziekenhuis Maastricht/Universiteit Maastricht, METC azM/UM (Maastricht)

Study registrations

Followed up by the following (possibly more current) registration

No registrations found.

Other (possibly less up-to-date) registrations in this register

ID: 29452
Source: NTR
Title:

In other registers

Register	ID
CCMO	NL57468.068.16
OMON	NL-OMON29452

Study results

Date completed: 19-11-2019

Actual enrolment: 48

Summary results
Trial is onging in other countries